FILE ORDERING
order patent files results

P

Friday (TGIF)
3/21/03
11:14:40 AM
WFO1003PR

Serial# 09/212082 File order accepted
Patent# 6048861
Serial# 09/453847 File order accepted
Patent# 6297249

Place another order

improper dep. clm
↑
+44
Claim 43 cannot be dependent
on
45-52 → improper dep. clm

L Number	Hits	Search Text	DB	Time stamp
1	855	(pyrimidine or pyrimidin or pyrimidinyl or pyrimidyl) and integrin	USPAT; US-PGPUB	2003/03/21 16:26

EAST

09/916,977

~~09/400,592~~ 9/916,977

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
NEWS 44	Feb 24	METADEX enhancements
NEWS 45	Feb 24	PCTGEN now available on STN
NEWS 46	Feb 24	TEMA now available on STN
NEWS 47	Feb 26	NTIS now allows simultaneous left and right truncation

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 NEWS 48  Feb 26  PCTFULL now contains images
 NEWS 49  Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
 NEWS 50  Mar 19  APOLLIT offering free connect time in April 2003
 NEWS 51  Mar 20  EVENTLINE will be removed from STN

 NEWS EXPRESS  January 6 CURRENT WINDOWS VERSION IS V6.01a,
               CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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FILE 'HOME' ENTERED AT 13:25:25 ON 21 MAR 2003

=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:25:33 ON 21 MAR 2003
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STRUCTURE FILE UPDATES:   20 MAR 2003  HIGHEST RN 500187-96-2
DICTIONARY FILE UPDATES:  20 MAR 2003  HIGHEST RN 500187-96-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09400992.str

L1      STRUCTURE UPLOADED
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~~09/=400,938~~

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=> d l1
L1 HAS NO ANSWERS
L1                STR
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G1 C,N,Ak


Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 13:25:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  29565 TO ITERATE

  3.4% PROCESSED    1000 ITERATIONS                                 12 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       581048 TO   601552
PROJECTED ANSWERS:            5965 TO     8225

L2            12 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 13:25:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 593732 TO ITERATE

 67.4% PROCESSED  400000 ITERATIONS                             5877 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.13

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       593732 TO   593732
PROJECTED ANSWERS:            8443 TO     9003

L3          5877 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               148.15     148.36

FILE 'CAPLUS' ENTERED AT 13:26:13 ON 21 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
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09/~~400,992~~

FILE COVERS 1907 - 21 Mar 2003 VOL 138 ISS 13
FILE LAST UPDATED: 20 Mar 2003 (20030320/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l3
L4        1325 L3

=> s l3/biol
          1325 L3
       5357235 BIOL/RL
L5         552 L3/BIOL
                (L3 (L) BIOL/RL)

=> s l3/thu
          1325 L3
        497792 THU/RL
L6         '320 L3/THU
                (L3 (L) THU/RL)

=> s l5 and integrin?
         23200 INTEGRIN?
L7          40 L5 AND INTEGRIN?

=> d l7 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 40 ANSWERS - CONTINUE? Y/(N):y

L7   ANSWER 1 OF 40  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:977654  CAPLUS
DOCUMENT NUMBER:          138:61306
TITLE:                    Preparation of pharmaceuticals containing
                          (pyrimidinyl)tetrahydronaphthyridinylnonanoic acid
                          Tris salt as an integrin receptor antagonist
INVENTOR(S):              Humphrey, Guy R.; Xu, Wei
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 21 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002102374      A1   20021227       WO 2002-US18906  20020614
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2003004171      A1   20030102       US 2002-174016   20020618
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PRIORITY APPLN. INFO.: US 2001-299344P P 20010619

AB The tris(hydroxymethyl)aminomethane ("TRIS") salt of 3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]-naphthyridin-2-yl)nonanoic acid is a potent antagonist of the **integrin** .alpha.v.beta.3 receptor and is useful for the prevention and/or treatment of osteoporosis and vascular restenosis, as well as conditions assocd. with excessive angiogenesis, such as macular degeneration, diabetic retinopathy, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. The invention also relates to a process for the prepn. of the salt as well as pharmaceutical compns. contg. the salt and methods of using the salt. Thus, the 3R or 3S isomer of 3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]-naphthyridin-2-yl)nonanoic acid was treated with tris(hydroxymethyl)aminomethane in EtOH soln. to give the title salts. The products were characterized by x-ray diffraction and FT-IR spectra and DSC. A 100-mg tablet is composed of 133 mg the active ingredient, 243 mg lactose, 20 mg croscarmellose sodium, and 4 mg magnesium stearate.

IT **479063-88-2P 479063-90-6P 479063-93-9P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of pharmaceuticals contg. (pyrimidinyl)tetrahydronaphthyridinyl nonanoic acid Tris salt as **integrin** receptor antagonist)

RN 479063-88-2 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

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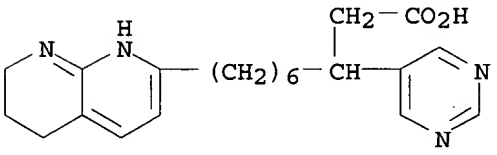
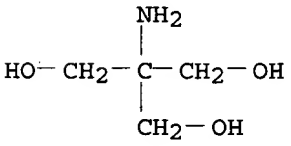
CRN 227753-43-7
CMF C21 H28 N4 O2



CM 2

CRN 77-86-1
CMF C4 H11 N O3



RN 479063-90-6 CAPLUS

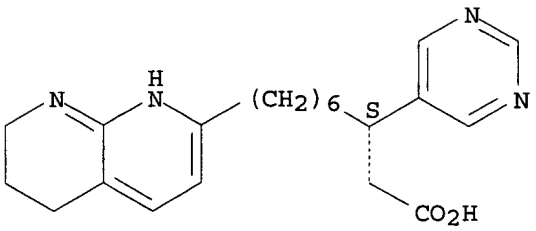
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 227752-24-1
CMF C21 H28 N4 O2

09/400,992

Absolute stereochemistry.



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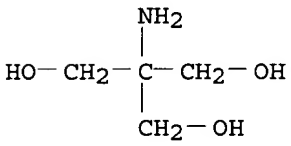
CRN 77-86-1
CMF C4 H11 N O3

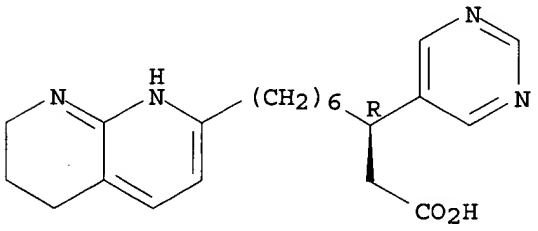


RN 479063-93-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 227752-23-0
CMF C21 H28 N4 O2

Absolute stereochemistry.



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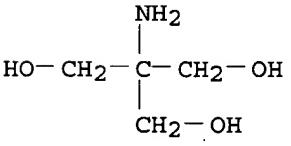
CRN 77-86-1
CMF C4 H11 N O3



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

~~09/ 400,992~~

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:736230 CAPLUS
DOCUMENT NUMBER: 137:263060
TITLE: Preparation of heterocyclic compounds as .alpha.v.beta.3 **integrin** inhibitors
INVENTOR(S): Morie, Toshiya; Iwama, Seiji; Notake, Mitsue; Kitano, Tomoko
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074743	A1	20020926	WO 2002-JP2391	20020314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-79029 A 20010319
OTHER SOURCE(S): MARPAT 137:263060

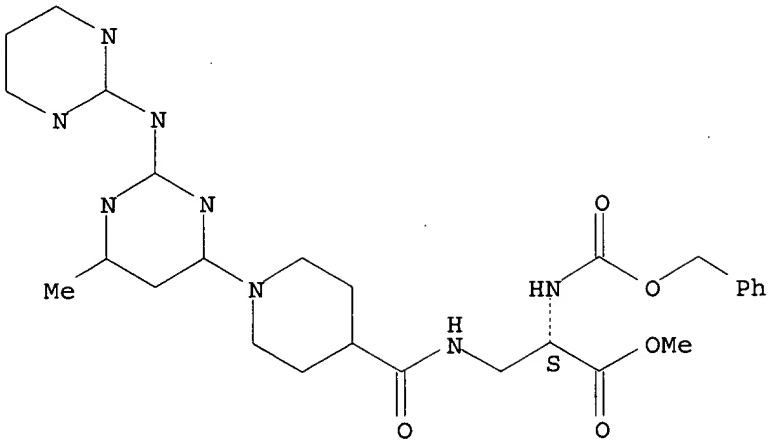
AB The title compds. UN(R3)ABZCH(R5)CH(R6)CO2R7 [U represents 1,4,5,6-tetrahydropyrimidine-2-yl group or the like, A represents a phenylene group or the like, B represents piperidine-1,4-diyl group or the like, Z represents CONH or the like, R3 represents hydrogen or the like, R5 represents hydrogen, an aryl group or the like, R6 represents a monosubstituted amino group, such as a benzyloxycarbonyl amino group, or the like, and R7 represents hydrogen or the like] are prepd. In an in vitro test for .alpha.v.beta.3 **integrin** binding inhibition, compds. of this invention showed IC50 values of 0.041 nM to 5.1 nM.

IT **461719-70-0P 461719-71-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of heterocyclic compds. as .alpha.v.beta.3 **integrin** inhibitors)

RN 461719-70-0 CAPLUS
CN L-Alanine, 3-[[[1-[6-methyl-2-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]-4-pyrimidinyl]-4-piperidinyl]carbonyl]amino]-N-[(phenylmethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~



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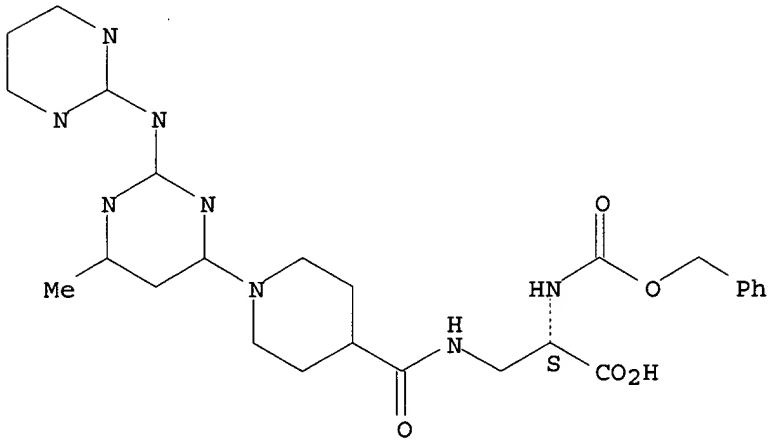
RN 461719-71-1 CAPLUS
CN L-Alanine, 3-[[[1-[6-methyl-2-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]-4-pyrimidinyl]-4-piperidinyl]carbonyl]amino]-N-[(phenylmethoxy)carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:409266 CAPLUS
DOCUMENT NUMBER: 136:409377
TITLE: Preparation of amine salts of an **integrin** receptor antagonist
INVENTOR(S): Humphrey, Guy R.; Waters, Marjorie See; Xu, Wei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

~~09/400,992~~

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002065291	A1	20020530	US 2001-998416	20011129
US 6444680	B2	20020903		

PRIORITY APPLN. INFO.: US 2000-250268P P 20001130

AB Amine salts of 3-(2-methyl-pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]-naphthyridin-2-yl)nonanoic acid are potent antagonists of the **integrin** .alpha.v.beta.3 receptor and are useful for the prevention and/or treatment of osteoporosis and vascular restenosis, as well as conditions assocd. with excessive angiogenesis, such as macular degeneration, diabetic retinopathy, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. The invention also relates to a process for the prepn. of the novel salts as well as pharmaceutical compns. contg. the salts and methods of using the salts. Also disclosed are 3(R)- and 3(S)-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)nonanoic acid (I) in the form of a zwitterion trihydrate. Thus, I were prepd. in a series of steps. A 100-mg tablet was composed of 100 mg active ingredient, 276 mg mannitol, 20 mg of croscarmellose sodium, and 4 mg magnesium stearate.

IT **431040-45-8P 431040-46-9P 431040-47-0P**
431040-48-1P 431040-49-2P 431040-50-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of amine salts of **integrin** receptor antagonist)

RN 431040-45-8 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

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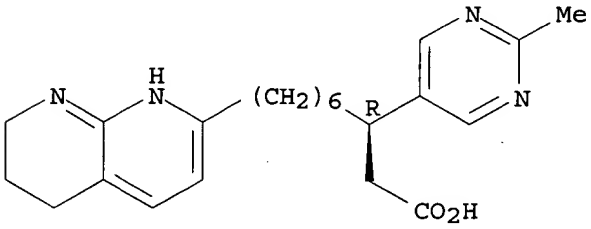
CRN 227753-48-2
CMF C22 H30 N4 O2

Absolute stereochemistry.



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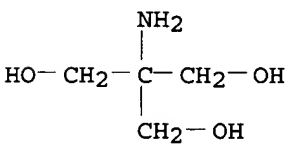
CRN 77-86-1
CMF C4 H11 N O3



RN 431040-46-9 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-

propanediol (1:1) (9CI) (CA INDEX NAME)

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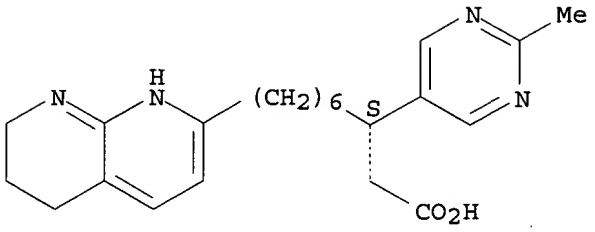
CRN 227753-49-3
CMF C22 H30 N4 O2

Absolute stereochemistry.



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CRN 77-86-1
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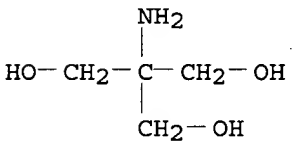
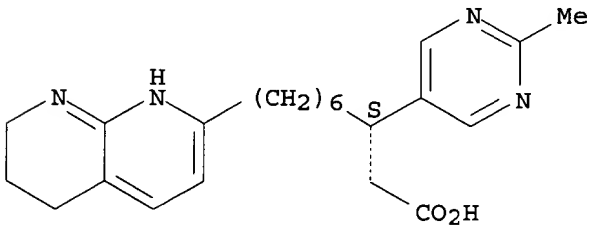
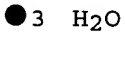


RN 431040-47-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, trihydrate, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

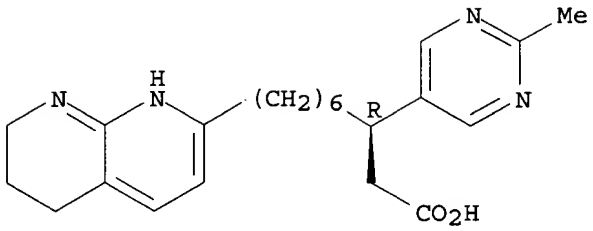




RN 431040-48-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, trihydrate, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,092~~



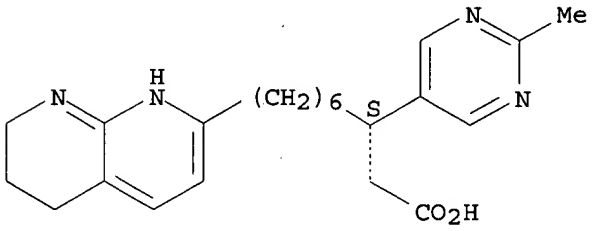
● 3 H_2O

RN 431040-49-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)-, compd. with 2-amino-2-methyl-1-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

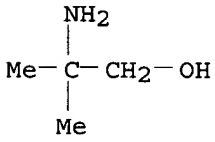
CRN 227753-49-3
CMF C22 H30 N4 O2

Absolute stereochemistry.



CM 2

CRN 124-68-5
CMF C4 H11 N O



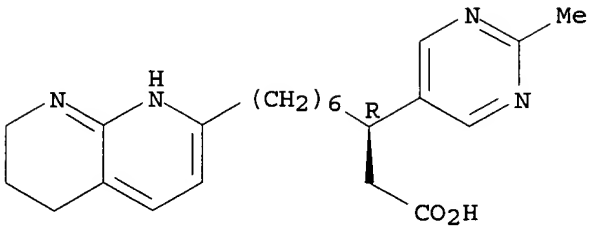
RN 431040-50-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, compd. with 2-amino-2-methyl-1-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 227753-48-2
CMF C22 H30 N4 O2

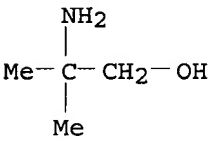
Absolute stereochemistry.

~~09/400,992~~



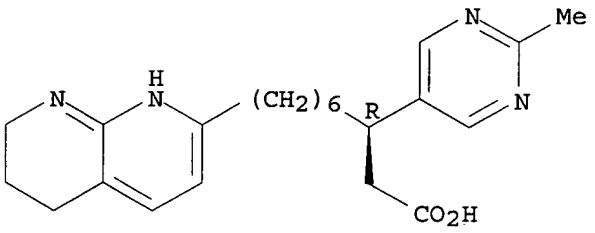
CM 2

CRN 124-68-5
CMF C4 H11 N O



IT **431040-51-6P 431040-52-7P 431040-53-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of amine salts of **integrin** receptor antagonist)
RN 431040-51-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, monoammonium salt, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



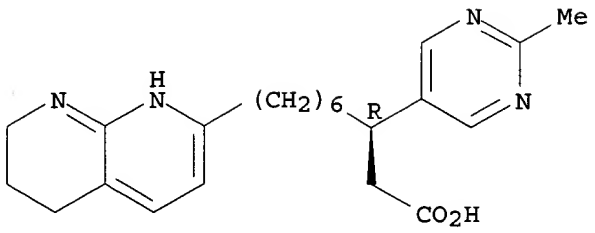
RN 431040-52-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, compd. with 1,2-ethanediamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 227753-48-2
CMF C22 H30 N4 O2

Absolute stereochemistry.

~~09/400,992~~



CM 2

CRN 107-15-3
CMF C2 H8 N2

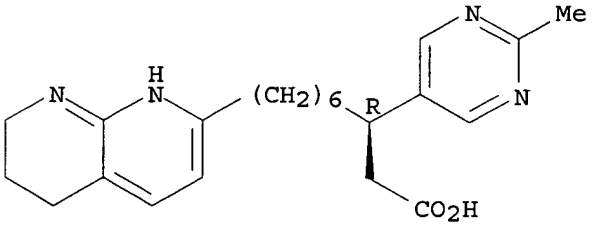
$H_2N-CH_2-CH_2-NH_2$

RN 431040-53-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, compd. with N-(phenylmethyl)benzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 227753-48-2
CMF C22 H30 N4 O2

Absolute stereochemistry.



CM 2

CRN 103-49-1
CMF C14 H15 N

$Ph-CH_2-NH-CH_2-Ph$

L7 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:349146 CAPLUS
DOCUMENT NUMBER: 136:369608
TITLE: Preparation of 3-(N'-oxodihydropyridinylureido)-3-phenylpropanoates as inhibitors of .alpha.4.beta.1 **integrin** binding
INVENTOR(S): Biediger, Ronald J.; Chen, Qi; Holland, George W.; Kassir, Jamal M.; Li, Wen; Market, Robert V.; Scott, Ian L.; Wu, Chengde; Decker, Radford E.; Li, Jian

~~09/400,992~~

PATENT ASSIGNEE(S): Texas Biotechnology Corporation, USA
SOURCE: Eur. Pat. Appl., 131 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1203766	A2	20020508	EP 2001-125494	20011106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2001005394	A	20020507	NO 2001-5394	20011105

PRIORITY APPLN. INFO.: US 2000-707068 A 20001106
US 2001-973142 A 20011009

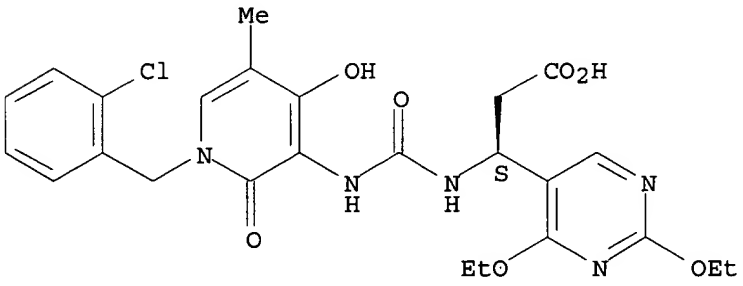
OTHER SOURCE(S): MARPAT 136:369608

AB Title compds. were prepd. Thus, 2-ClC6H4CH2ZNH2 (Z = 4-ethyl-2-oxo-1,2-dihydropyridine-1,3-diyl)(prepn. given) was condensed with (S)-4-MeC6H4CH(NH2)CH2CO2Et and COCl2 to give, after sapon., (S)-2-ClC6H4CH2ZNHCONHCH(C6H4Me-4)CH2CO2H (Z as above). Data for biol. activity of title compds. were given.

IT **422516-89-0P 422517-60-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of 3-(N'-oxodihydropyridinylureido)-3-phenylpropanoates as inhibitors of .alpha.4.beta.1 **integrin** binding)

RN 422516-89-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[[[[1-[(2-chlorophenyl)methyl]-1,2-dihydro-4-hydroxy-5-methyl-2-oxo-3-pyridinyl]amino]carbonyl]amino]-2,4-diethoxy-, (.beta.S)- (9CI) (CA INDEX NAME)

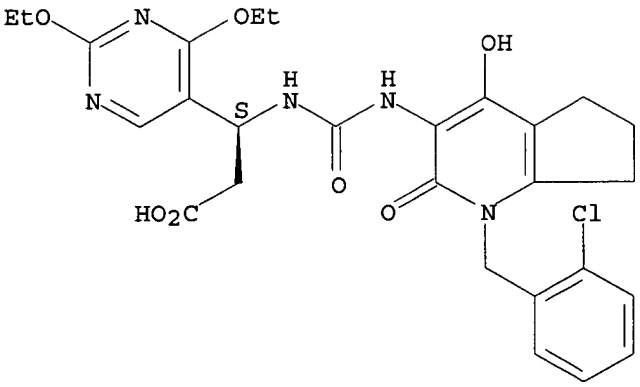
Absolute stereochemistry.



RN 422517-60-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[[[[1-[(2-chlorophenyl)methyl]-2,5,6,7-tetrahydro-4-hydroxy-2-oxo-1H-cyclopenta[b]pyridin-3-yl]amino]carbonyl]amino]-2,4-diethoxy-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/ 400,992~~



L7 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:275794 CAPLUS
DOCUMENT NUMBER: 136:309803
TITLE: Preparation of a phosphoric acid salt of an **integrin** receptor antagonist
INVENTOR(S): Meissner, Robert S.; Xu, Wei
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028395	A1	20020411	WO 2001-US30647	20011001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001096439	A5	20020415	AU 2001-96439	20011001

PRIORITY APPLN. INFO.: US 2000-237534P P 20001004
WO 2001-US30647 W 20011001

GI

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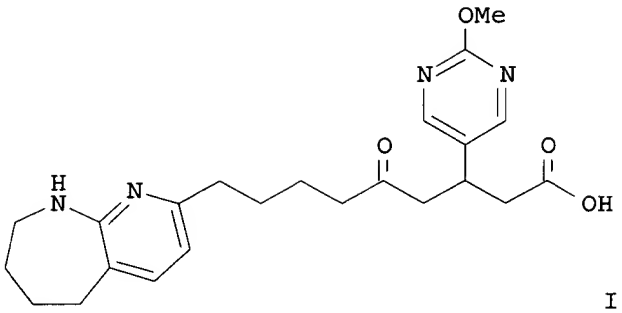


I

AB The phosphoric acid salt of 3-(2-methoxy-pyrimidin-5-yl)-5-oxo-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin- -yl)-nonanoic acid (I) is a potent antagonist of the **integrin** .alpha..nu..beta.3 receptor and is useful for the prevention and/or treatment of osteoporosis and vascular restenosis, as well as conditions assocd. with excessive angiogenesis, such as macular degeneration, diabetic retinopathy, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. The invention also relates to a process for the prepn. of the novel salt as well as pharmaceutical compns. and methods of use. Thus, I.cntdot.H3PO4 was prepd. from I Et ester via sapon. with aq. NaOH followed by reaction of H3PO4 in EtOH. The the crystal structure of I.cntdot.H3PO4 was detd. via x-ray powder diffraction.

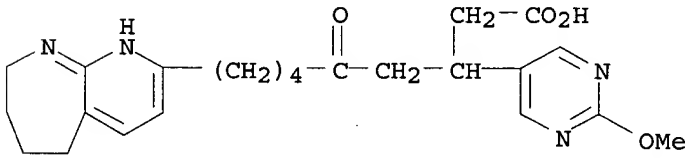
IT **408357-11-9P 408357-12-0P 408357-13-1P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of cryst. phosphoric acid salt of **integrin** .alpha..nu..beta.3 receptor antagonist useful as therapeutic for osteoporosis and vascular restenosis)

RN 408357-11-9 CAPLUS

CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

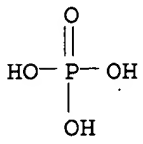
CRN 312262-23-0
CMF C23 H30 N4 O4



CM 2

CRN 7664-38-2
CMF H3 O4 P

~~09/400,992~~

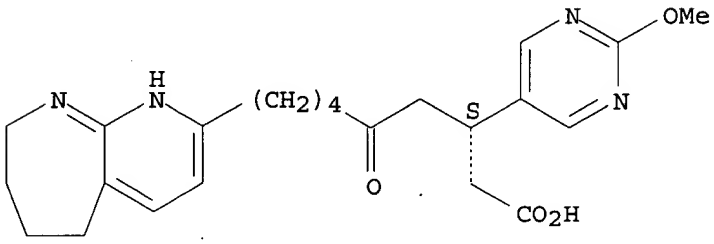


RN 408357-12-0 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

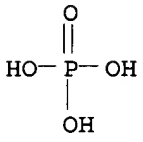
CRN 312262-25-2
CMF C23 H30 N4 O4

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P



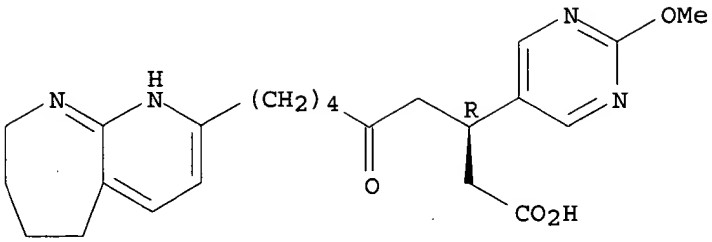
RN 408357-13-1 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 312262-24-1
CMF C23 H30 N4 O4

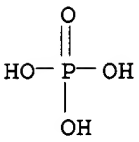
Absolute stereochemistry.

~~09/400,992~~



CM 2

CRN 7664-38-2
CMF H3 O4 P



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

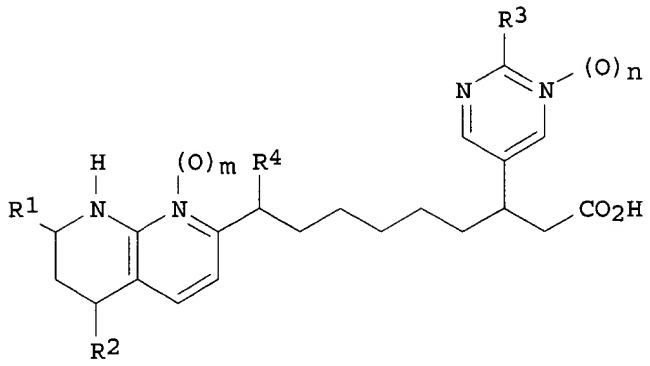
L7 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220592 CAPLUS
DOCUMENT NUMBER: 136:263170
TITLE: Pyrimidinylnaphthyridinenonanoic acid derivatives as .alpha.v.beta.3 **integrin** receptor antagonists
INVENTOR(S): Coleman, Paul J.; Cui, Donghui; Duggan, Mark E.; Fang, Xiaojun; Hutchinson, John H.; Prueksaritanont, Thomayant; Silva Elipe, Maria Victoria
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022616	A2	20020321	WO 2001-US28404	20010910
WO 2002022616	A3	20020606		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090772	A5	20020326	AU 2001-90772	20010910
US 2002040030	A1	20020404	US 2001-953606	20010914

PRIORITY APPLN. INFO.: US 2000-232262P P 20000914
WO 2001-US28404 W 20010910

~~09/400,992~~

OTHER SOURCE(S): MARPAT 136:263170
GI



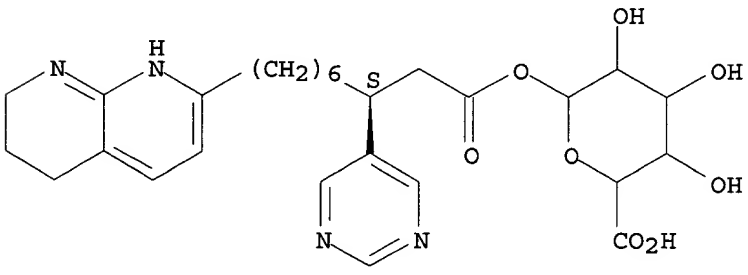
I

AB The title compds. I [R1, R2, R4 = H, OH, O; R3 = H, Me; m, n = 0, 1], formed by metabolic conversion of I [R1, R2, R4 = H; R3 = H, Me; m, n = 0] with rat liver microsomes, are .alpha.v.beta.3 **integrin** receptor antagonists. They are particularly useful for inhibiting bone resorption and for the treatment and prevention of osteoporosis. Thus, I [R1, R2, R4 = H, R3 = Me, m, n = 0] was prepd. and was incubated with rat liver microsomes for 2.5 h at 37.degree.C to yield I [R1, R4 = H, R2 = OH, R3 = Me, m, n = 0; R1 = O, OH, R2, R4 = H, R3 = Me, m, n = 0;R1, R2 = H, R3 = Me, R4 = OH, m, n = 0; R1, R2, R4 = H, R3 = Me, m = 0, n = 1; R1, R2, R4 = H, R3 = Me, m = 1, n = 0] and the 5,6,7,8-tetradehydro analog of I [R1, R2, R4 = H, R3 = Me, m, n = 0]. The products had IC50 <100nM in the SPAV3 assay.

IT **405061-24-7 405061-25-8**
RL: BSU (Biological study, unclassified); **BIOL (Biological study)** (metabolite formed from pyrimidinylnaphthyridinenonanoic acid .alpha.v.beta.3 **integrin** receptor antagonists)

RN 405061-24-7 CAPLUS
CN .beta.-D-Glucopyranuronic acid, 1-[(.beta.S)-1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-1,8-naphthyridine-2-nonanoate] (9CI) (CA INDEX NAME)

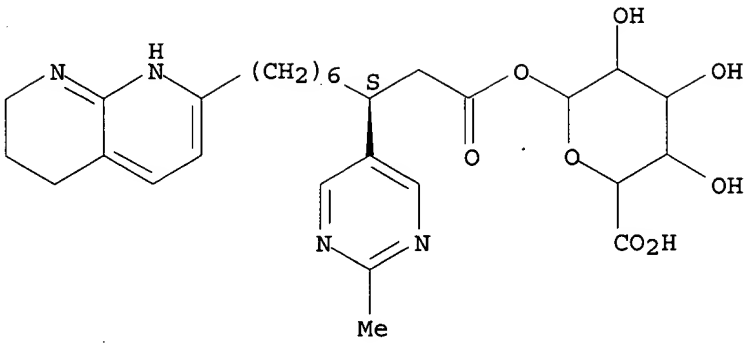
Absolute stereochemistry.



RN 405061-25-8 CAPLUS
CN .beta.-D-Glucopyranuronic acid, 1-[(.beta.S)-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-1,8-naphthyridine-2-nonanoate] (9CI) (CA INDEX NAME)

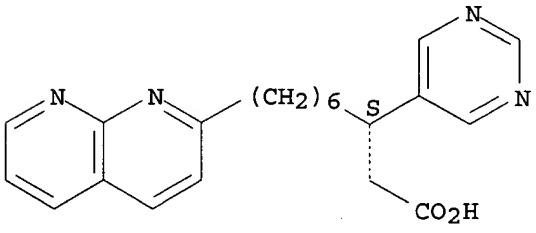
Absolute stereochemistry.

~~09/400,992~~



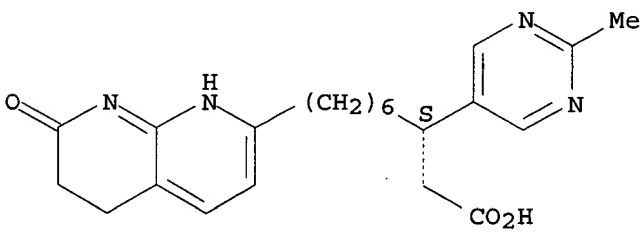
IT **404869-57-4**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); **BIOL (Biological study)**; USES (Uses)
(metabolite formed from pyrimidinylnaphthyridinenonanoic acid .alpha.v.beta.3 **integrin** receptor antagonists)
RN 404869-57-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **404869-73-4P 404869-75-6P 404869-76-7P 404869-78-9P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of metabolites formed from pyrimidinylnaphthyridinenonanoic acid .alpha.v.beta.3 **integrin** receptor antagonists)
RN 404869-73-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-7-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 404869-75-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-7-hydroxy-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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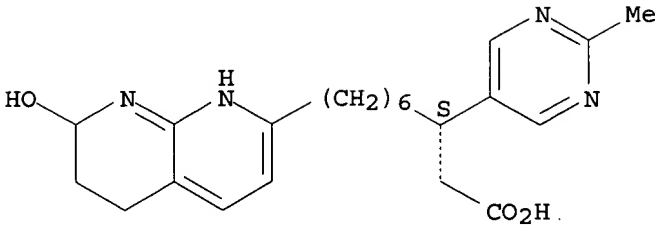
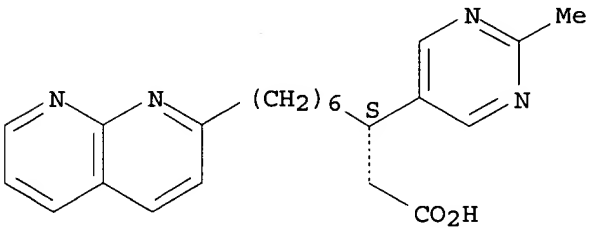


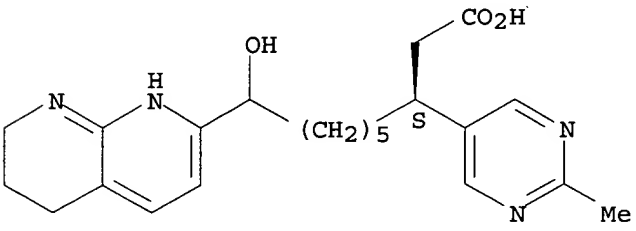
RN 404869-76-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



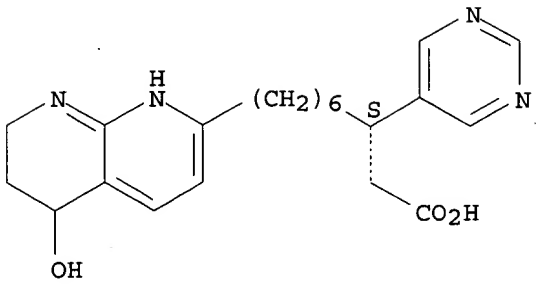
RN 404869-78-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.theta.-hydroxy-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



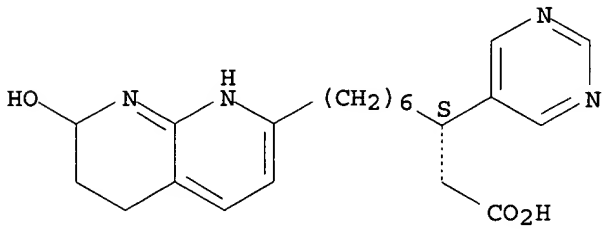
IT **404869-56-3P 404869-85-8P 404869-86-9P**
404869-87-0P 404869-88-1P
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of pyrimidinylnaphthyridinenonanoic acid derivs. as .alpha.v.beta.3 **integrin** receptor antagonists)
RN 404869-56-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-5-hydroxy-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



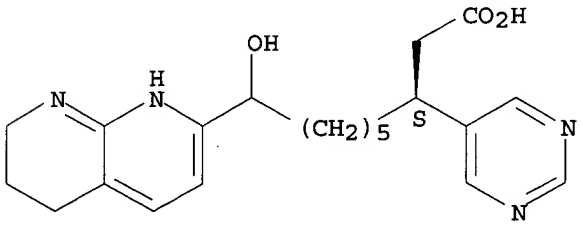
RN 404869-85-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-7-hydroxy-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



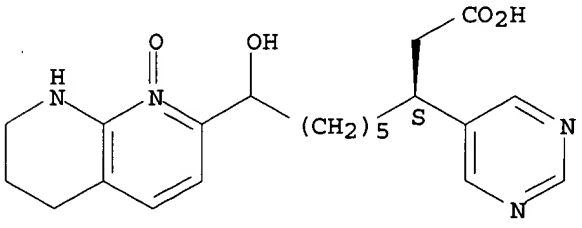
RN 404869-86-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.theta.-hydroxy-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 404869-87-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 5,6,7,8-tetrahydro-.theta.-hydroxy-.beta.-5-pyrimidinyl-, 1-oxide, (.beta.S)- (9CI) (CA INDEX NAME)

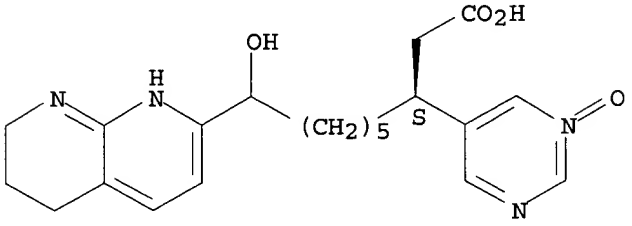
Absolute stereochemistry.



RN 404869-88-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.theta.-hydroxy-

.beta.-(1-oxido-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

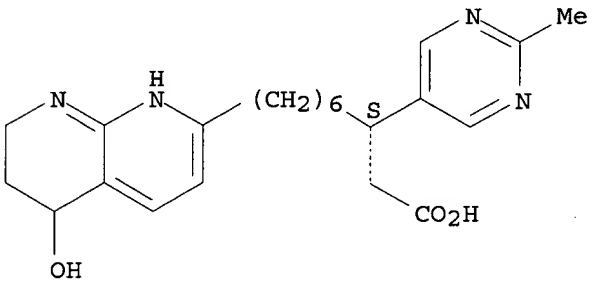
Absolute stereochemistry.



IT **404869-70-1P 404869-80-3P 404869-82-5P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of pyrimidinylnaphthyridinenonanoic acid derivs. as .alpha.v.beta.3 **integrin** receptor antagonists)

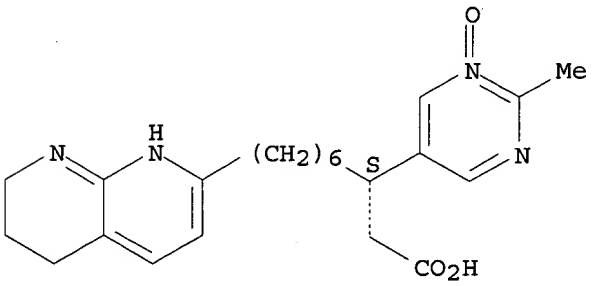
RN 404869-70-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-5-hydroxy-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 404869-80-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-1-oxido-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 404869-82-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, 1-oxide, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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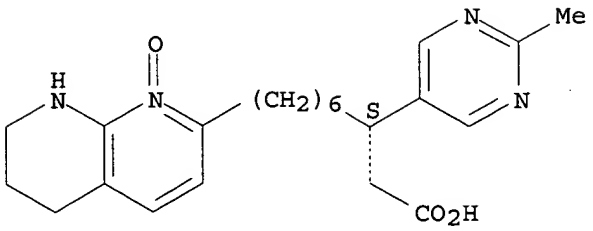
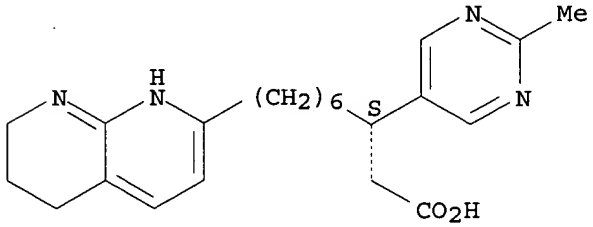


IT **227753-49-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of pyrimidinylnaphthyridinenonanoic acid derivs. as .alpha.v.beta.3 **integrin** receptor antagonists)
RN 227753-49-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

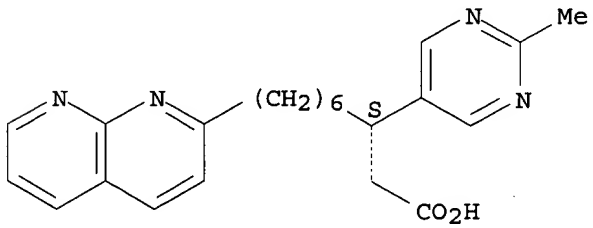


IT **404869-83-6P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of pyrimidinylnaphthyridinenonanoic acid derivs. as .alpha.v.beta.3 **integrin** receptor antagonists)
RN 404869-83-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 404869-76-7
CMF C22 H26 N4 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1

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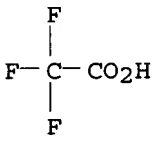
CMF C2 H F3 O2



L7 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220369 CAPLUS
DOCUMENT NUMBER: 136:241665
TITLE: Treatment of inflammation with a combination of a cyclooxygenase-2 inhibitor and an **integrin** alpha-V antagonist
INVENTOR(S): Hartman, George; Duggan, Mark; Rodan, Gideon A.; Rodan, Sevgi B.; Duong, Le T.; Kimmel, Donald B.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

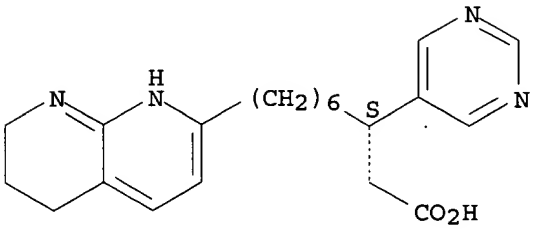
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022124	A1	20020321	WO 2001-US42146	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001095038	A5	20020326	AU 2001-95038	20010914
US 2002040039	A1	20020404	US 2001-955379	20010918

PRIORITY APPLN. INFO.: US 2000-233609P P 20000918
WO 2001-US42146 W 20010914
OTHER SOURCE(S): MARPAT 136:241665

AB The present invention provides for methods for treating or preventing an inflammatory disease or condition in a mammalian patient in need of such treatment comprising administering to said patient a cyclooxygenase-2 specific inhibitor in combination with an .alpha.V.beta.3, .alpha.V.beta.5, and/or .alpha.V.beta.6 **integrin** receptor antagonist in an amt. effective to treat or prevent the inflammatory disease or condition. The present invention also provides for pharmaceutical compns. for the treatment or prevention of an inflammatory disease or condition. Further, the invention provides for the manuf. of a medicament useful in the treatment or prevention of an inflammatory disease or condition.

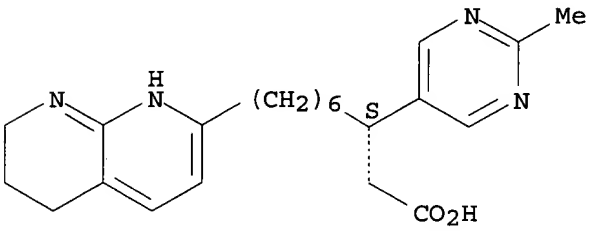
IT **227752-24-1 227753-49-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); **BIOL (Biological study)**; USES (Uses)
(treatment of inflammation with a combination of a cyclooxygenase-2 inhibitors and an **integrin**-.alpha.V antagonists)
RN 227752-24-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 227753-49-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:90040 CAPLUS
DOCUMENT NUMBER: 136:135022
TITLE: Preparation of heteroaryl-.beta.-alanine derivatives as antiinflammatory agents and .alpha.4 **integrin** inhibitors
INVENTOR(S): Konradi, Andrei W.; Pleiss, Michael A.; Thorsett, Eugene D.; Ashwell, Susan; Welmaker, Gregory S.; Kreft, Anthony; Sarantakis, Dimitrios; Dressen, Darren B.; Grant, Francine S.; Semko, Christopher; Xu, Ying-Zi
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008222	A2	20020131	WO 2001-US23096	20010720
WO 2002008222	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

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DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002086882 A1 20020704 US 2001-910431 20010719

PRIORITY APPLN. INFO.: US 2000-220128P P 20000721

OTHER SOURCE(S): MARPAT 136:135022

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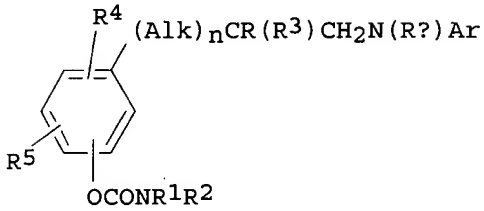

I

AB Disclosed are a series of heteroaryl-.beta.-alanine derivs. I wherein R is a carboxylic acid; R1 and R2 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, or R1 and R2, together with the nitrogen atom to which they are attached, are joined to form an optionally substituted heterocyclic ring provided that said substituted alkyl, substituted alkenyl and substituted cycloalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; Ra and R3 are independently a hydrogen or a Me group; R4 and R5 are independently selected from the group consisting of heteroatom group; n is zero or an integer 1; Alk is a straight or branched alkylene chain; Ar is an optionally substituted arom. or heteroarom. group, as well as their pharmaceutical use as .alpha.4.beta.7 **Integrin** inhibitors for the treatment of inflammatory diseases. Thus, 3-[4-(3,5-dichloropyrid-4-ylcarboxamido)phenyl]-2-(3-chlorophenylamino)propanoic acid was prepd. as .alpha.4 **Integrin** inhibitor. The preferred compds. of the invention generally have IC50 values in the .alpha.4.beta.1 and .alpha.a.beta.7 assays of 1 .mu.M and below. In the other assays featuring .alpha. **integrins** of other subgroups the same compds. had IC50 values of 50 .mu.M and above thus demonstrating the potency and selectivity of their action against .alpha.4 **integrins**. Title compds. were prepd. for treating an inflammatory condition in a mammalian patient which condition is mediated by Very Late Antigen 4 (VLA-4). Inflammatory condition is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia and acute leukocyte-mediated lung injury.

IT **263275-13-4P 263275-14-5P**

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)

(prepn. of heteroaryl-.beta.-alanine derivs. as antiinflammatory agents and .alpha.4 **integrin** inhibitors)

RN 263275-13-4 CAPLUS

CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.alpha.-[[[6-(propylsulfonyl)-4-pyrimidinyl]amino]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

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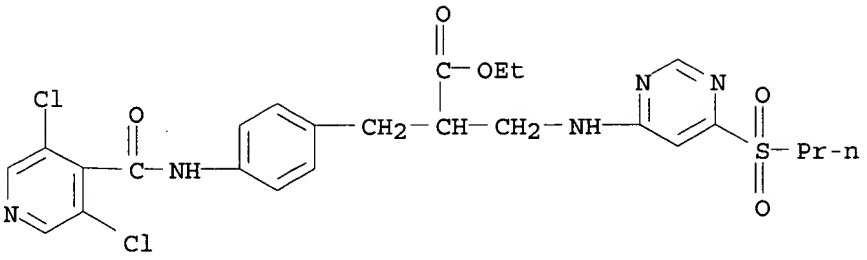
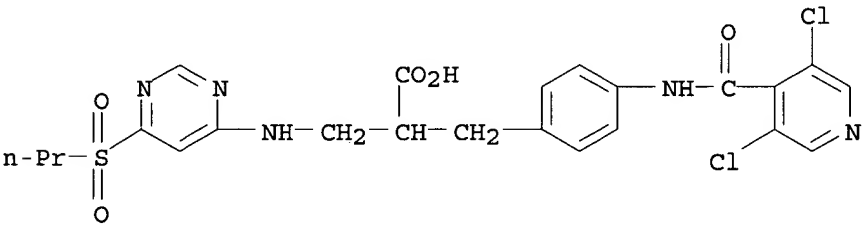


RN 263275-14-5 CAPLUS
CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.alpha.-[[[6-(propylsulfonyl)-4-pyrimidinyl]amino]methyl]- (9CI) (CA INDEX NAME)



L7 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:90026 CAPLUS
DOCUMENT NUMBER: 136:135019
TITLE: Preparation of 3-amino-2-(4-aminocarbonyloxy)phenyl-propionic acid derivatives as antiinflammatory agents and .alpha.4 **Integrin** inhibitors
INVENTOR(S): Konradi, Andrei W.; Pleiss, Michael A.; Thorsett, Eugene D.; Ashwell, Susan; Welmaker, Gregory S.; Kreft, Anthony; Sarantakis, Dimitrios; Dressen, Darren B.; Grant, Francine S.; Xu, Ying-Zi
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008206	A1	20020131	WO 2001-US23073	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002055509	A1	20020509	US 2001-910685	20010720

PRIORITY APPLN. INFO.: US 2000-220134P P 20000721
OTHER SOURCE(S): MARPAT 136:135019

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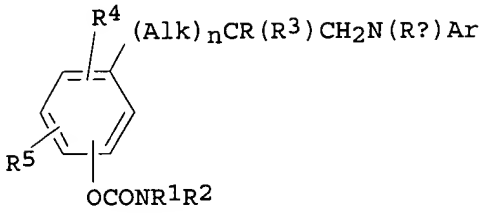
GI



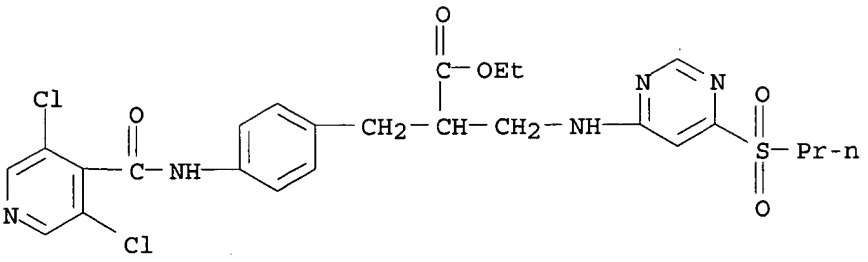
I

AB 3-Amino-2-(4-aminocarbonyloxy)phenyl-propionic acid derivs. I wherein R is a carboxylic acid; R1 and R2 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, or R1 and R2, together with the nitrogen atom to which they are attached, are joined to form an optionally substituted heterocyclic ring provided that said substituted alkyl, substituted alkenyl and substituted cycloalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; Ra and R3 are independently a hydrogen or a Me group; R4 and R5 are independently selected from the group consisting of heteroatom group; n is zero or an integer 1; Alk is a straight or branched alkylene chain; Ar is an optionally substituted arom. or heteroarom. group, as well as their pharmaceutical use as .alpha.4.beta.7 **Integrin** inhibitors for the treatment of inflammatory diseases. Thus, 3-[4-(3,5-dichloropyrid-4-ylcarboxamido)phenyl]-2-(3-chlorophenylamino)propanoic acid was prepd. as .alpha.4 **Integrin** inhibitor. The preferred compds. of the invention generally have IC50 values in the .alpha.4.beta.1 and .alpha.a.beta.7 assays of 1 .mu.M and below. In the other assays featuring .alpha. **integrins** of other subgroups the same compds. had IC50 values of 50 .mu.M and above thus demonstrating the potency and selectivity of their action against .alpha.4 **integrins**. Title compds. were prepd. for treating an inflammatory condition in a mammalian patient which condition is mediated by Very Late Antigen 4 (VLA-4). Inflammatory condition is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia and acute leukocyte-mediated lung injury.

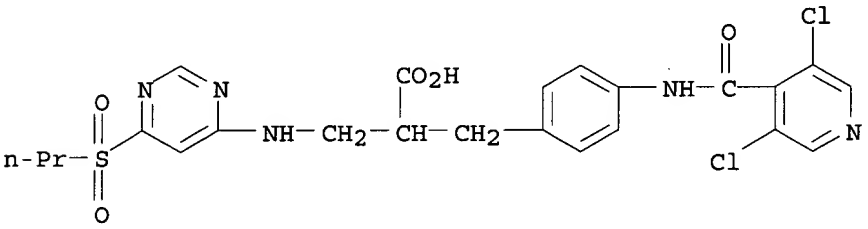
IT **263275-13-4P 263275-14-5P**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of aminoaminocarbonyloxyphenylpropionic acid derivs. as a **integrin** inhibitors)

RN 263275-13-4 CAPLUS

CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.alpha.-[[[6-(propylsulfonyl)-4-pyrimidinyl]amino]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 263275-14-5 CAPLUS
CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.alpha.-[[[6-(propylsulfonyl)-4-pyrimidinyl]amino]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

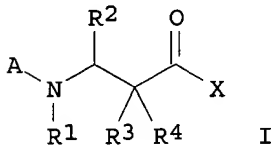
L7 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:90021 CAPLUS
DOCUMENT NUMBER: 136:135017
TITLE: Prepn. of beta-amino acid derivatives as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Konradi, Andrei W.; Pleiss, Michael A.; Thorsett, Eugene D.; Ashwell, Susan; Welmaker, Gregory S.; Kreft, Anthony; Sarantakis, Dimitrios; Grant, Francine S.; Dressen, Darren B.; Semko, Christopher; Xu, Ying-Zi; Stappenbeck, Frank
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008201	A2	20020131	WO 2001-US23071	20010720
WO 2002008201	A3	20020627		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

~~09/400,992~~

US 2002058664 A1 20020516 US 2001-909838 20010720
PRIORITY APPLN. INFO.: US 2000-220118P P 20000721
OTHER SOURCE(S): MARPAT 136:135017
GI



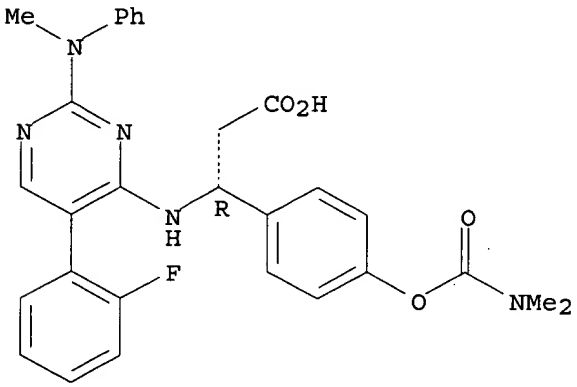
I

AB Beta-amino acid derivs. I [R1 = H, (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, heteroaryl, or heterocyclic; R3 and R4 = H, halogen, alkyl, substituted alkyl, alkenyl, alkynyl, alkoxy, haloalkoxy, alkylthio, alkylamino, alkylcyano, etc.; X = OH, (un)substituted alkoxy, alkenoxy, cycloalkoxy, cycloalkenoxy, aryloxy, heteroaryloxy, heterocyclyloxy, amino, etc.; A = (un)substituted aryl, heteroaryl, cycloalkyl, or heterocyclic group; R2 = acylamino, acyloxy, (un)substituted acyl(hetero)aryl, aminoacyl(hetero)aryl, aminocarbonylamino(hetero)aryl, etc.] were prepd. as as inhibitors of leukocyte adhesion mediated by VLA-4. Compds. I have IC50 of 15 .mu.M or less in assay for detg. binding to VLA-4. Thus, (R)-3-[(5-(2-fluorophenyl)-2-(N-cyclohexyl-N-methylamino]-pyrimidin-4-ylamino)-3-(4-(dimethylaminocarbonyl)oxyphenyl)propanoic acid was prepd. from p-hydroxycinnamate and (S)-(-)-benzyl-.alpha.-methylbenzylamine by multistep procedure via coupling of (R)-3-amino-3-(4-tert-butyldimethylsiloxy)phenyl)-propanoic acid Et ester with 2,4-dichloro-5-bromopyrimidine.

IT **392662-81-6P 392662-83-8P 392662-84-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of beta-amino acid derivs. as inhibitors of leukocyte adhesion mediated by VLA-4)

RN 392662-81-6 CAPLUS
CN Benzenepropanoic acid, 4-[[(dimethylamino)carbonyl]oxy]-.beta.-[[5-(2-fluorophenyl)-2-(methylphenylamino)-4-pyrimidinyl]amino]-, (.beta.R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

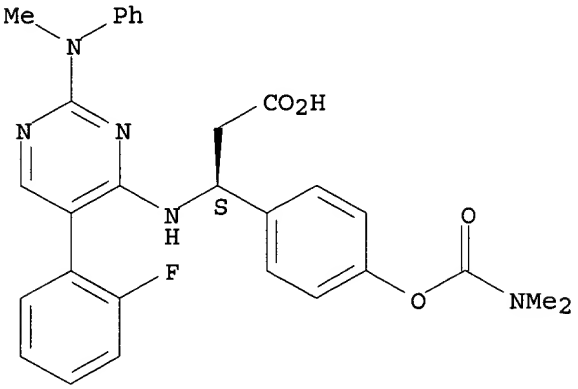


RN 392662-83-8 CAPLUS
CN Benzenepropanoic acid, 4-[[(dimethylamino)carbonyl]oxy]-.beta.-[[5-(2-fluorophenyl)-2-(methylphenylamino)-4-pyrimidinyl]amino]-, (.beta.S)-

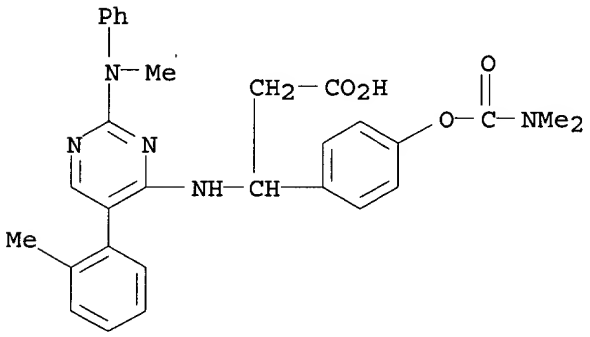
~~09/400,992~~

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 392662-84-9 CAPLUS
CN Benzenepropanoic acid, 4-[[(dimethylamino)carbonyl]oxy]-.beta.-[[5-(2-methylphenyl)-2-(methylphenylamino)-4-pyrimidinyl]amino]- (9CI) (CA INDEX NAME)



L7 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:89834 CAPLUS
DOCUMENT NUMBER: 136:134745
TITLE: Preparation of heterocycle-substituted chain-fluorinated carboxylic acids and esters useful as .alpha.v **integrin** receptor antagonists
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007730	A1	20020131	WO 2001-US22938	20010720

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-220903P P 20000726

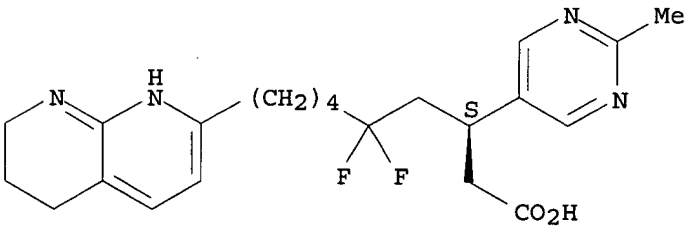
AB The present invention relates to novel chain-fluorinated alkanoic acid derivs. XCH2CH2CR32CH2CR42CH2CHR5CH2CO2R6 (1; e.g. (3S)-5,5-difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid), their synthesis, and their use as .alpha.v **integrin** receptor antagonists. More particularly, the compds. of the present invention are antagonists of the **integrin** receptors .alpha.v.beta.3 and/or .alpha.v.beta.5 and are useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammation, inflammatory arthritis, viral disease, cancer, and metastatic tumor growth. In 1, X = 5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl, 2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-2-yl, 5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl, or 6-R2NHpyridin-2-yl, wherein each nonarom. ring C atom is unsubstituted or independently substituted with one or two R1 substituents and each arom. ring C atom is unsubstituted or independently substituted with one R1 substituent. R1 = C1-8 alkyl, C3-8 cycloalkyl, C3-8 cycloheteroalkyl, C3-8 cycloalkyl-C1-6 alkyl, C3-8 cycloheteroalkyl-C1-6 alkyl, aryl, aryl-C1-6 alkyl, amino, amino-C1-6 alkyl, C1-3 acylamino, C1-3 acylamino-C1-6 alkyl, (C1-6 alkyl)1-2-amino, C3-6 cycloalkyl-C0-2 amino, (C1-6 alkyl)1-2-amino-C1-6-alkyl, C1-6 alkoxy, C1-4 alkoxy-C1-6 alkyl, hydroxycarbonyl, hydroxycarbonyl-C1-6 alkyl, C1-3 alkoxycarbonyl, C1-3 alkoxycarbonyl-C1-6 alkyl, hydroxy, hydroxy-C1-6-alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy, trifluoroethoxy, C1-8 alkyl-S(O)0-2, (C1-8 alkyl)0-2-aminocarbonyl, C1-8 alkyloxycarbonylamino, (C1-8 alkyl)1-2-aminocarbonyloxy, (aryl C1-3 alkyl)1-2-amino, (aryl)1-2-amino, aryl-C1-3 alkylsulfonylamino, and C1-8 alkylsulfonylamino; or two R1 substituents, when on the same nonarom. C atom, are taken together with the C atom to which they are attached to form a carbonyl group, or two R1 substituents, together with the nonarom. C atoms to which they are attached, join to form a 4- to 6-membered satd. or unsatd. carbocyclic ring. R2 is H or C1-4 alkyl; R3 is fluoro and R4 is H or R3 is H and R4 is fluoro. Although the methods of prepn. are not claimed, .apprx.10 example prepns. are included. Representative compds. of the present invention were tested and found to bind to human .alpha.v.beta.3 **integrin**. These compds. were generally found to have IC50 values <10 nM in the SPAV3 assay. Representative compds. of the present invention were also tested in the SPAV5 assay to det. affinity for the .alpha.v.beta.5 receptor. These compds. were generally found to have IC50 values <100 nM.

IT **393177-64-5P**, (3S)-5,5-Difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-68-9P**, (3R)-5,5-Difluoro-3-(2-Methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-70-3P**, (3S)-9-(3-Cyclopropyl-5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)-5,5-difluoro-3-(2-methylpyrimidin-5-yl)nonanoic acid **393177-74-7P**, (3R)-9-(3-Cyclopropyl-5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)-5,5-difluoro-3-(2-methylpyrimidin-5-yl)nonanoic acid **393177-75-8P**, (3S)-5,5-Difluoro-3-(2-Methoxypyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-79-2P**, (3R)-5,5-Difluoro-3-(2-Methoxypyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-89-4P**, 5,5-Difluoro-3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-90-7P**, (3S)-5,5-Difluoro-3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-91-8P**, (3R)-5,5-Difluoro-3-(pyrimidin-5-yl)-9-(5,6,7,8-

tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-92-9P**, 5,5-Difluoro-3-(2-methoxypyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-93-0P**, 5,5-Difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid **393177-94-1P**, 9-(3-Cyclopropyl-5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)-5,5-difluoro-3-(2-methylpyrimidin-5-yl)nonanoic acid **393177-95-2P**, 5,5-Difluoro-3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393177-96-3P**, (3S)-5,5-Difluoro-3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393177-97-4P**, (3R)-5,5-Difluoro-3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393177-98-5P**, 5,5-Difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393177-99-6P**, (3S)-5,5-Difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393178-00-2P**, (3R)-5,5-Difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393178-01-3P**, 5,5-Difluoro-3-(2-methoxypyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393178-02-4P**, (3S)-5,5-Difluoro-3-(2-methoxypyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid **393178-03-5P**, (3R)-5,5-Difluoro-3-(2-methoxypyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl)nonanoic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of heterocycle-substituted chain-fluorinated carboxylic acids and esters useful as .alpha.v **integrin** receptor antagonists)

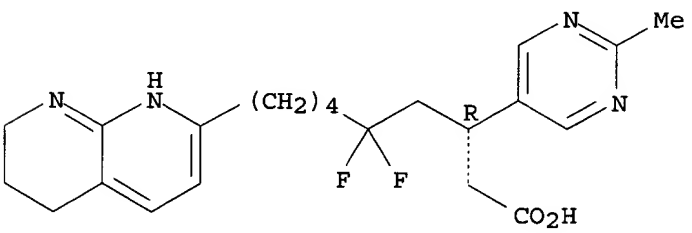
RN 393177-64-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



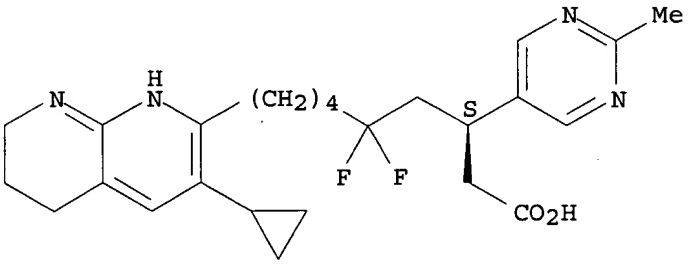
RN 393177-68-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



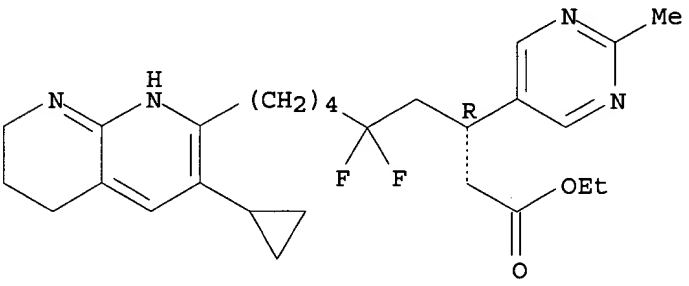
RN 393177-70-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-.delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



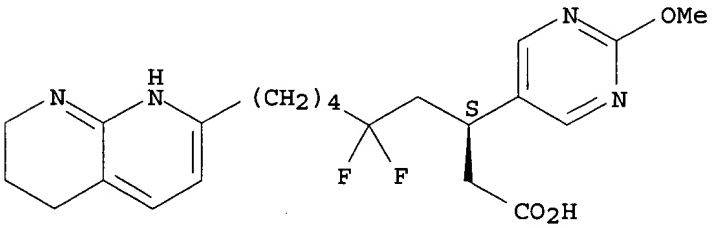
RN 393177-74-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-.delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, ethyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



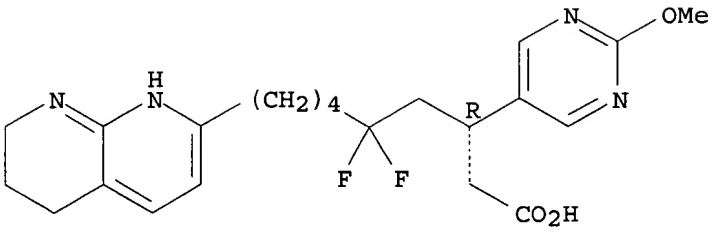
RN 393177-75-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

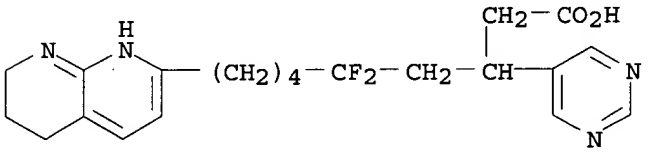


RN 393177-79-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

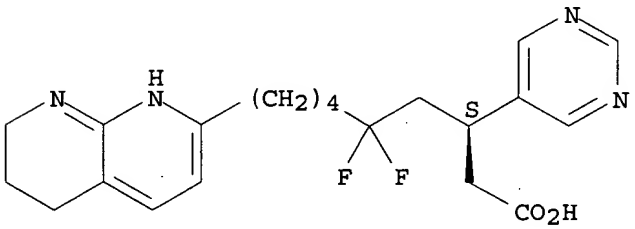


RN 393177-89-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl- (9CI) (CA INDEX NAME)



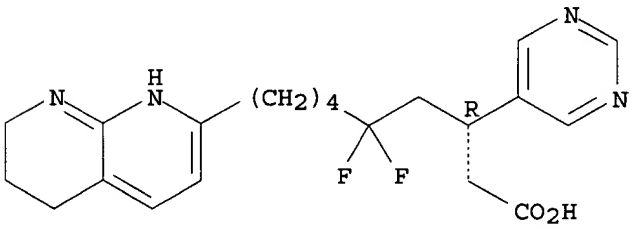
RN 393177-90-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

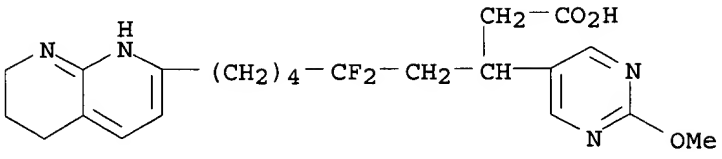


RN 393177-91-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

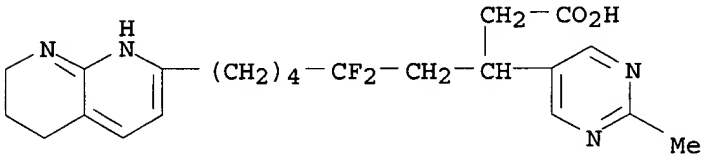
Absolute stereochemistry.



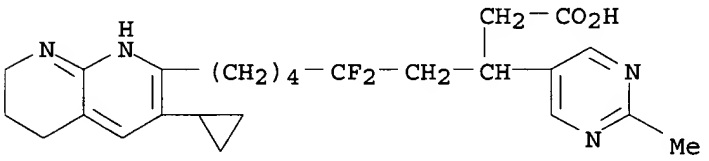
RN 393177-92-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



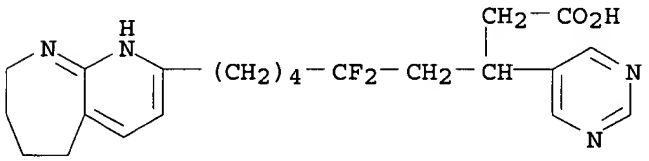
RN 393177-93-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 393177-94-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-.delta.,.delta.-difluoro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)

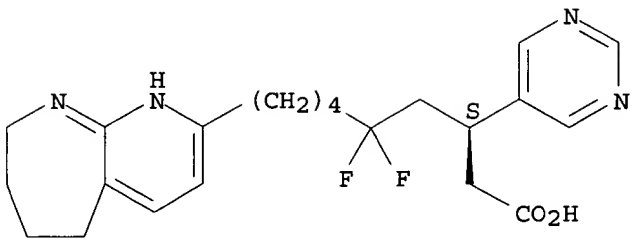


RN 393177-95-2 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-5-pyrimidinyl- (9CI) (CA INDEX NAME)



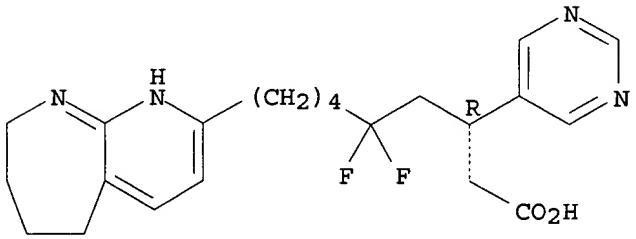
RN 393177-96-3 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

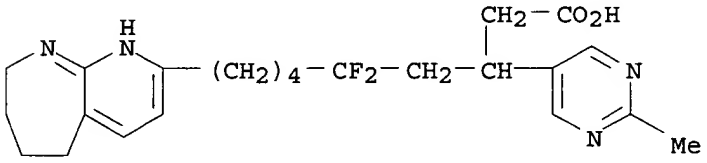


RN 393177-97-4 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

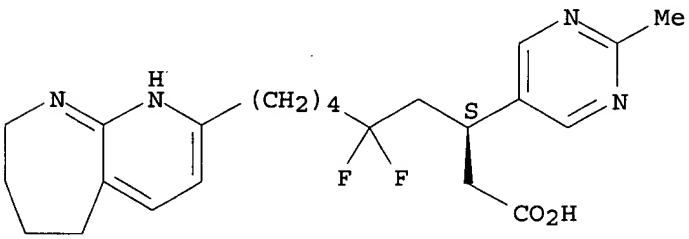


RN 393177-98-5 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 393177-99-6 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

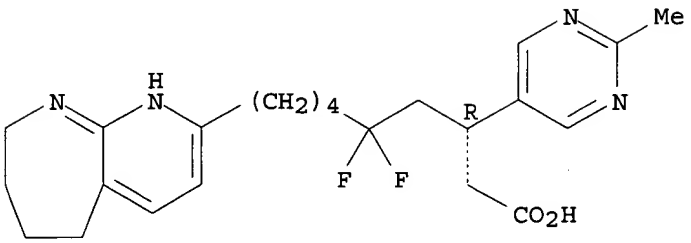
Absolute stereochemistry.



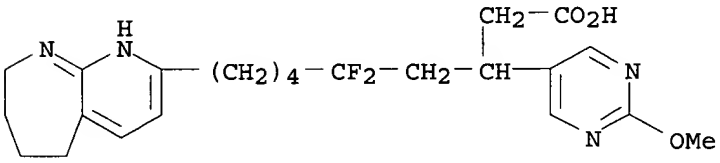
RN 393178-00-2 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.

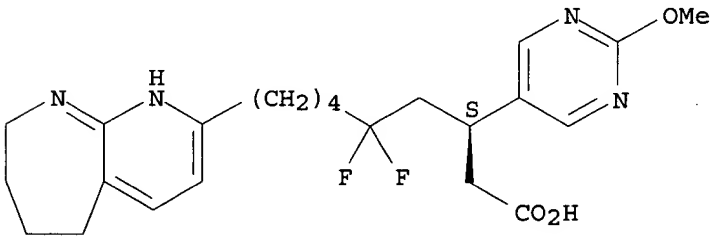


RN 393178-01-3 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



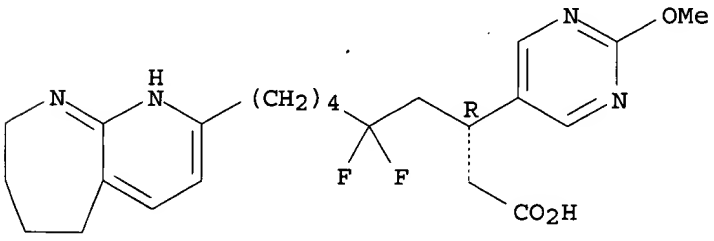
RN 393178-02-4 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 393178-03-5 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .delta.,.delta.-difluoro-5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



~~09/ 400,592~~

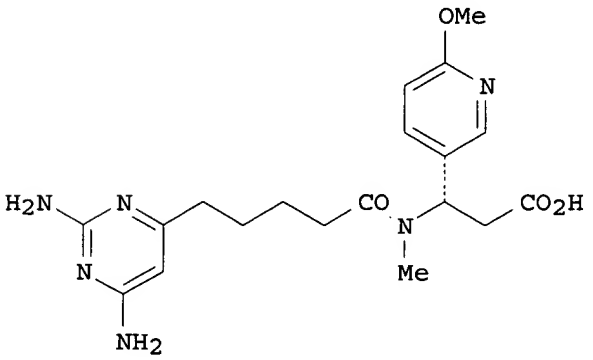
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:545664 CAPLUS
DOCUMENT NUMBER: 135:137514
TITLE: Preparation and formulation heterocyclyl-alkanoic acids for pharmaceutical use as **integrin** .alpha.v receptor antagonists
INVENTOR(S): Askew, Ben C.; Breslin, Michael J.; Duggan, Mark E.; Hutchinson, John H.; Meissner, Robert S.; Perkins, James J.; Steele, Thomas G.; Patane, Michael A.
PATENT ASSIGNEE(S): Merck + Co., Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053262	A1	20010726	WO 2001-US1953	20010119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1254116	A1	20021106	EP 2001-908643	20010119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2001053853	A1	20011220	US 2001-767471	20010123

PRIORITY APPLN. INFO.: US 2000-177792P P 20000124
US 2000-230469P P 20000906
WO 2001-US1953 W 20010119

OTHER SOURCE(S): MARPAT 135:137514
GI



I

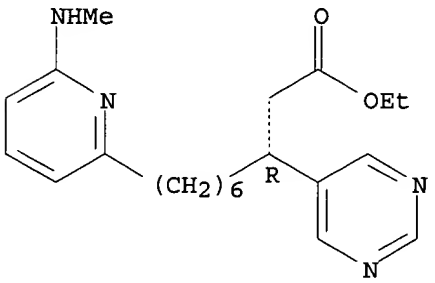
AB Heterocyclyl-alkanoic acids, such as X-(CH2)4-Y-CHR4CH2CO2R5 [X = nitrogen

contg. heterocyclyl, such as pyridinyl, pyrimidinyl, azaindolyl, etc.; Y = (CH2)2, CONR3; R3, R5 = H, alkyl; R4 = aryl or heteroaryl, such as Ph, naphthyl, furyl thienyl, imidazolyl, etc.] were prepd. as antagonists of the **integrin** receptors .alpha.v.beta.3 and/or .alpha..beta.5 and may be useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. Thus, the trifluoroacetic acid salt of heterocyclyl-alkanoic acid I was prepd. via a multistep synthetic sequence starting from 2-methoxypyridine, Et acrylate, Et 4-pentenoate, and 6-chloro-2,4-diaminopyrimidine. The prepd. acids were tested for **integrin** .alpha.v.beta.3 and .alpha..beta.5 binding activity and bone resorption activity. Examples of pharmaceutical formulations of the heterocyclyl-alkanoic acids were also presented.

IT **351447-25-1P 351447-26-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and formulation heterocyclyl-alkanoic acids for pharmaceutical use as **integrin** .alpha.v receptor antagonists)

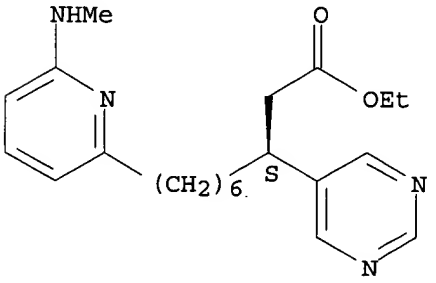
RN 351447-25-1 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, ethyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351447-26-2 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, ethyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



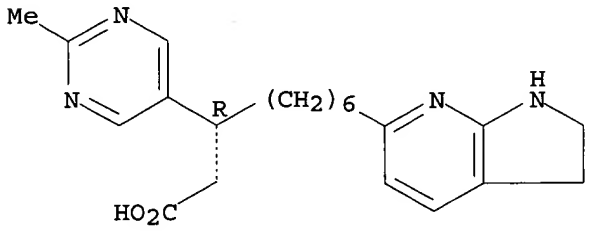
IT **351446-54-3P 351446-55-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. and formulation heterocyclyl-alkanoic acids for pharmaceutical

use as **integrin** .alpha.v receptor antagonists)

RN 351446-54-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-6-nonanoic acid, 2,3-dihydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

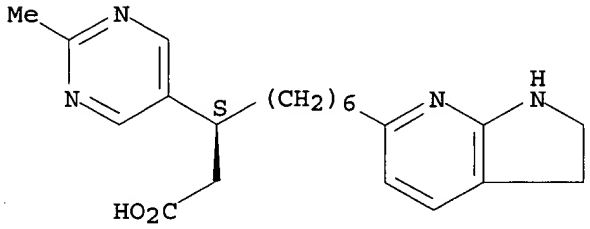
Absolute stereochemistry.



RN 351446-55-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-6-nonanoic acid, 2,3-dihydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

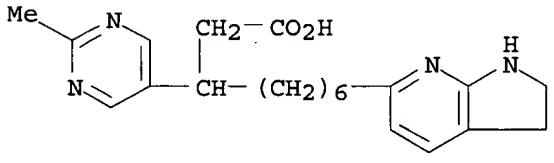
Absolute stereochemistry.



IT **351446-53-2P 351447-03-5P 351447-24-0P**
351447-33-1P 351447-37-5P 351447-50-2P
351447-96-6P 351447-97-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and formulation heterocyclyl-alkanoic acids for pharmaceutical use as **integrin** .alpha.v receptor antagonists)

RN 351446-53-2 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-6-nonanoic acid, 2,3-dihydro-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 351447-03-5 CAPLUS

CN 3-Pyridinepropanoic acid, .beta.-[[5-(2,6-diamino-4-pyrimidinyl)-1-oxopentyl]methylamino]-6-methoxy-, ethyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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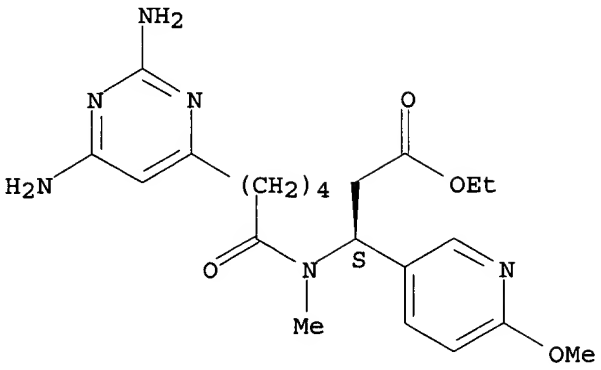
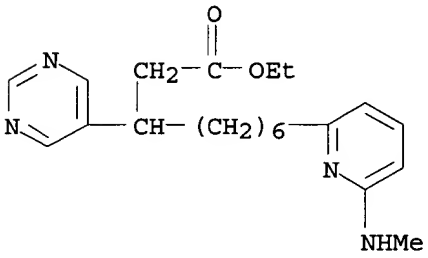
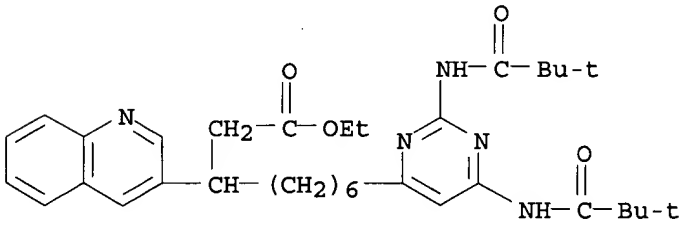


RN 351447-24-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, ethyl ester (9CI) (CA INDEX NAME)

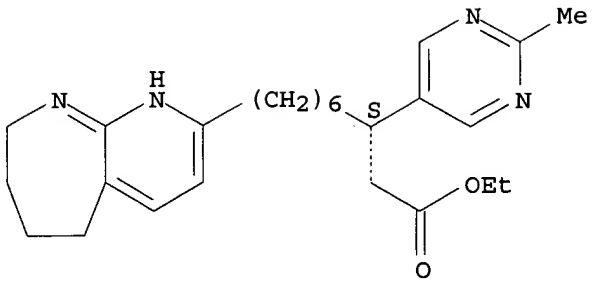


RN 351447-33-1 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-[6-[2,6-bis[(2,2-dimethyl-1-oxopropyl)amino]-4-pyrimidinyl]hexyl]-, ethyl ester (9CI) (CA INDEX NAME)



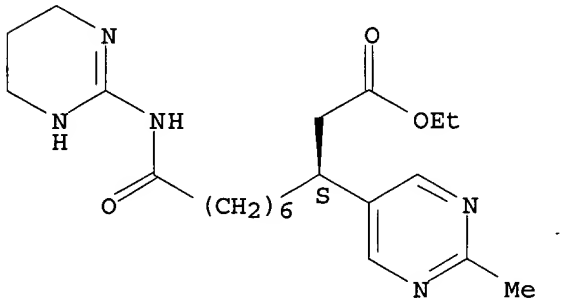
RN 351447-37-5 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, ethyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

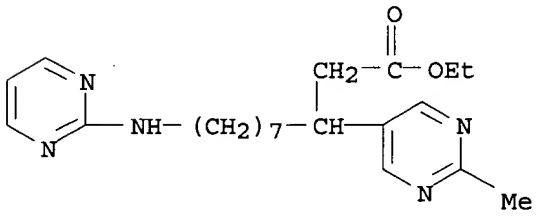


RN 351447-50-2 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-oxo-7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]-, ethyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

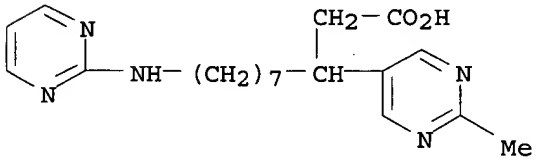
Absolute stereochemistry.



RN 351447-96-6 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-(2-pyrimidinylamino)heptyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 351447-97-7 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-(2-pyrimidinylamino)heptyl]- (9CI) (CA INDEX NAME)



IT **351445-89-1P 351445-90-4P 351445-95-9P 351445-96-0P 351445-98-2P 351446-00-9P**

351446-01-0P 351446-03-2P 351446-05-4P
351446-07-6P 351446-11-2P 351446-12-3P
351446-13-4P 351446-14-5P 351446-15-6P
351446-16-7P 351446-17-8P 351446-18-9P
351446-19-0P 351446-20-3P 351446-21-4P
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351446-89-4P 351446-92-9P 351446-93-0P
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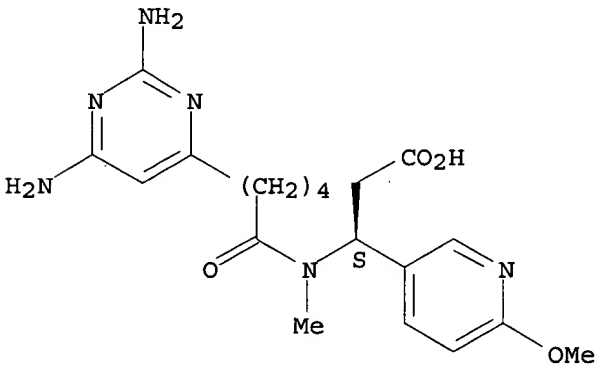
351496-31-6P 351496-32-7P 351496-33-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. and formulation heterocyclyl-alkanoic acids for pharmaceutical use as **integrin** .alpha.v receptor antagonists)

RN 351445-89-1 CAPLUS
CN 3-Pyridinepropanoic acid, .beta.-[[5-(2,6-diamino-4-pyrimidinyl)-1-oxopentyl]methylamino]-6-methoxy-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

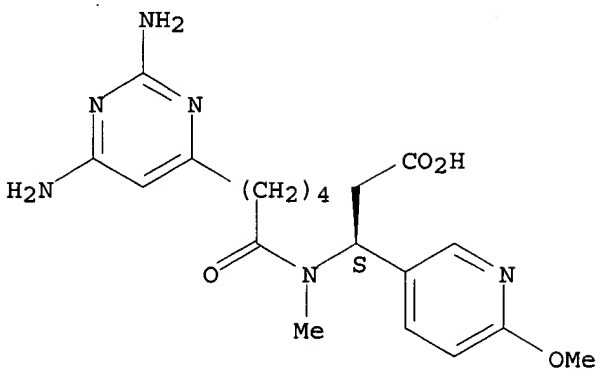


RN 351445-90-4 CAPLUS
CN 3-Pyridinepropanoic acid, .beta.-[[5-(2,6-diamino-4-pyrimidinyl)-1-oxopentyl]methylamino]-6-methoxy-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

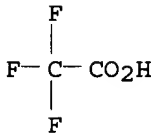
CRN 351445-89-1
CMF C19 H26 N6 O4

Absolute stereochemistry.



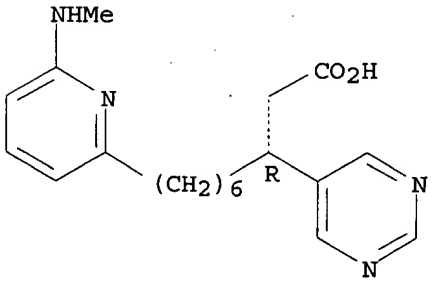
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351445-95-9 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

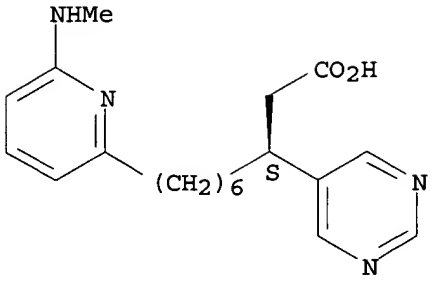
Absolute stereochemistry.



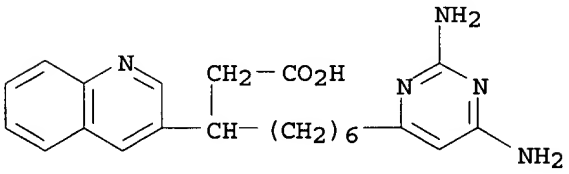
RN 351445-96-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~98/400,992~~

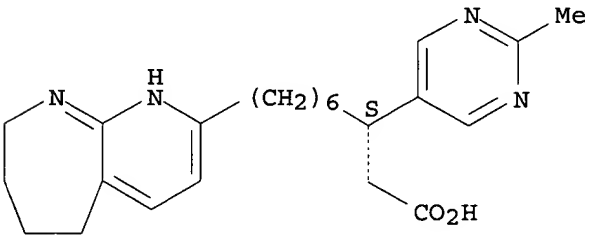


RN 351445-98-2 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-[6-(2,6-diamino-4-pyrimidinyl)hexyl]- (9CI) (CA INDEX NAME)



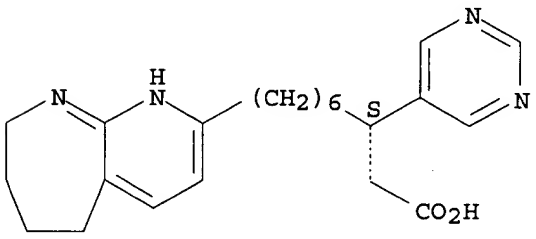
RN 351446-00-9 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



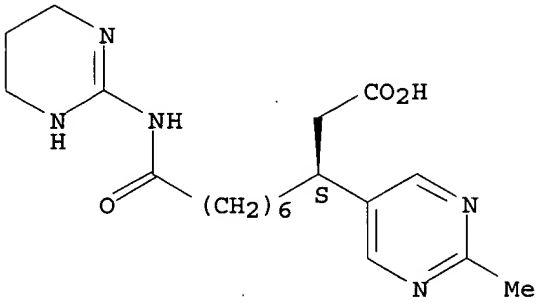
RN 351446-01-0 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



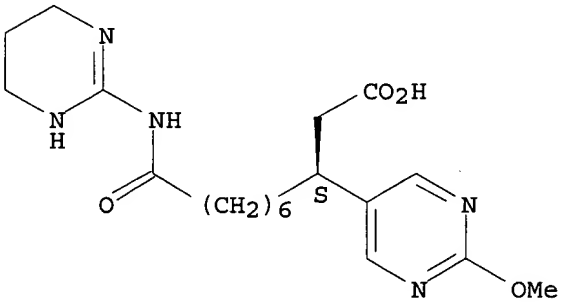
RN 351446-03-2 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-oxo-7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



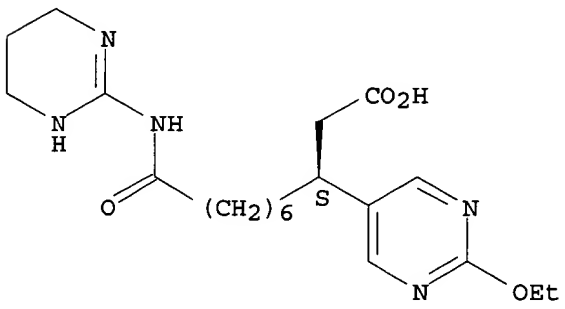
RN 351446-05-4 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methoxy-.beta.-[7-oxo-7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351446-07-6 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[7-oxo-7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

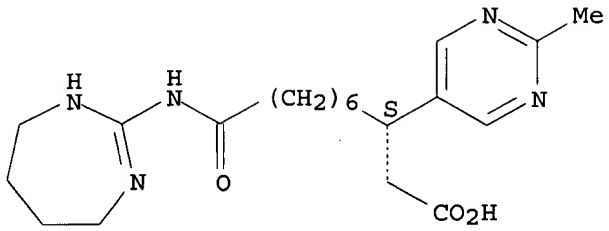
Absolute stereochemistry.



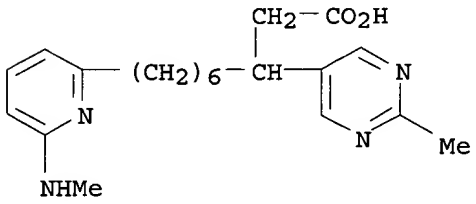
RN 351446-11-2 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-oxo-7-[(4,5,6,7-tetrahydro-1H-1,3-diazepin-2-yl)amino]heptyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

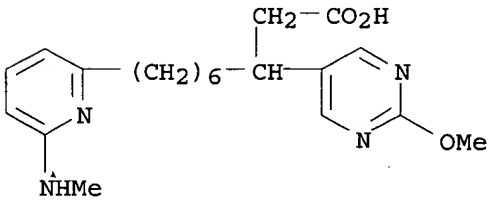
~~09/400,992~~



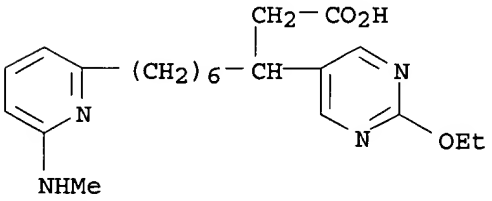
RN 351446-12-3 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]- (9CI) (CA INDEX NAME)



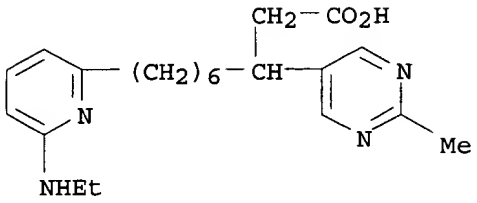
RN 351446-13-4 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methoxy-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]- (9CI) (CA INDEX NAME)



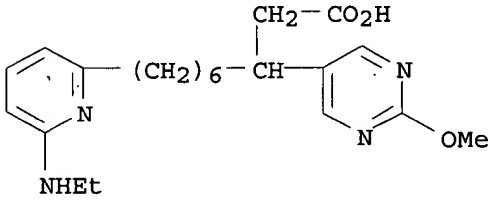
RN 351446-14-5 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]- (9CI) (CA INDEX NAME)



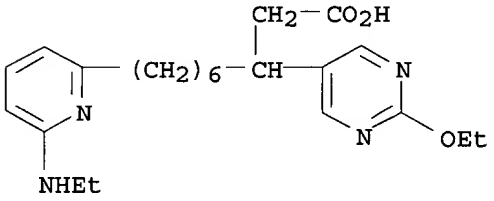
RN 351446-15-6 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-2-methyl- (9CI) (CA INDEX NAME)



RN 351446-16-7 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-2-methoxy- (9CI) (CA INDEX NAME)

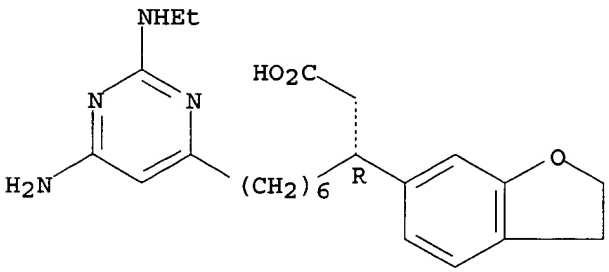


RN 351446-17-8 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]- (9CI) (CA INDEX NAME)



RN 351446-18-9 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2,3-dihydro-6-benzofuranyl)-2-(ethylamino)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351446-19-0 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2,3-dihydro-6-benzofuranyl)-2-(ethylamino)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

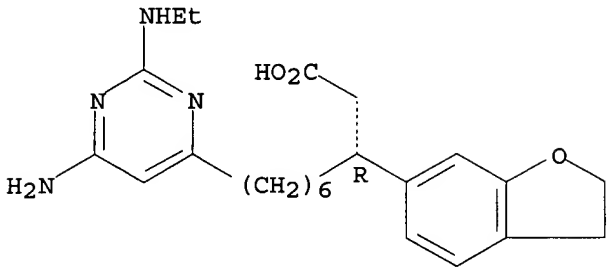
CM 1

CRN 351446-18-9

~~09/400,992~~

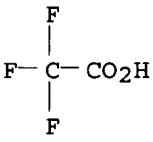
CMF C23 H32 N4 O3

Absolute stereochemistry.



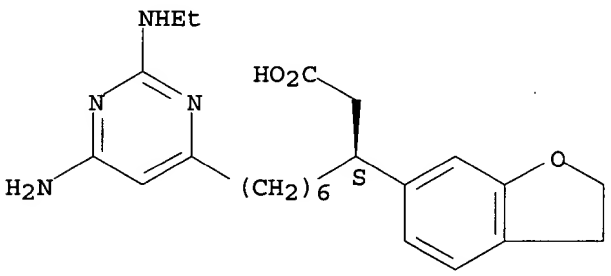
CM 2

CRN 76-05-1
CMF C2 H F3 O2



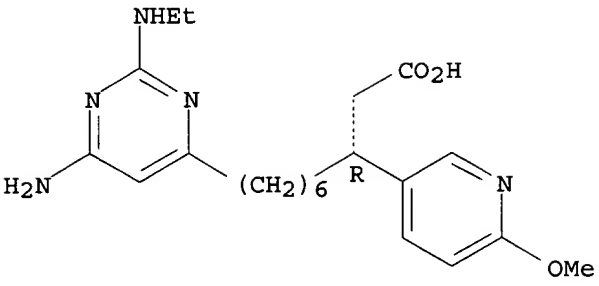
RN 351446-20-3 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2,3-dihydro-6-benzofuranyl)-2-(ethylamino)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351446-21-4 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(6-methoxy-3-pyridinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

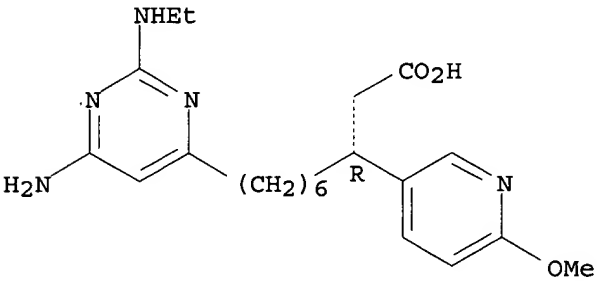


RN 351446-22-5 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(6-methoxy-3-pyridinyl)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

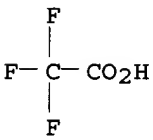
CRN 351446-21-4
CMF C21 H31 N5 O3

Absolute stereochemistry.



CM 2

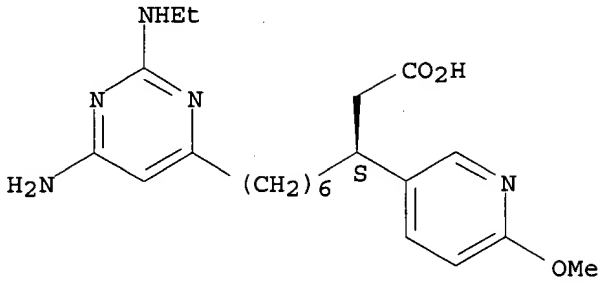
CRN 76-05-1
CMF C2 H F3 O2



RN 351446-23-6 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(6-methoxy-3-pyridinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~

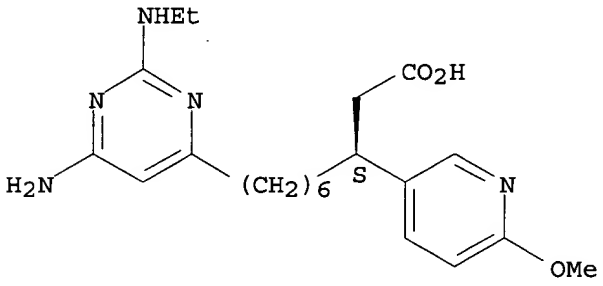


RN 351446-24-7 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(6-methoxy-3-pyridinyl)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

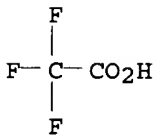
CRN 351446-23-6
CMF C21 H31 N5 O3

Absolute stereochemistry.



CM 2

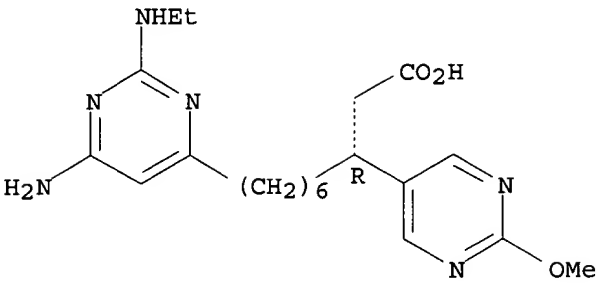
CRN 76-05-1
CMF C2 H F3 O2



RN 351446-25-8 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~

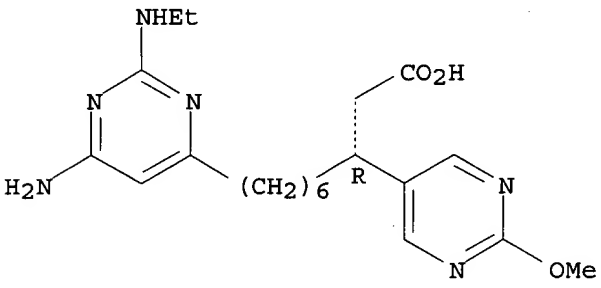


RN 351446-26-9 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

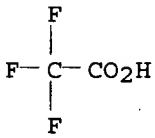
CRN 351446-25-8
CMF C20 H30 N6 O3

Absolute stereochemistry.



CM 2

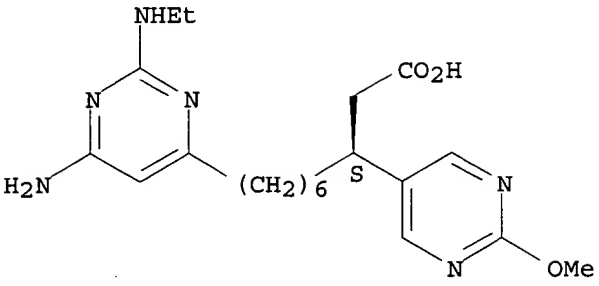
CRN 76-05-1
CMF C2 H F3 O2



RN 351446-27-0 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,892~~

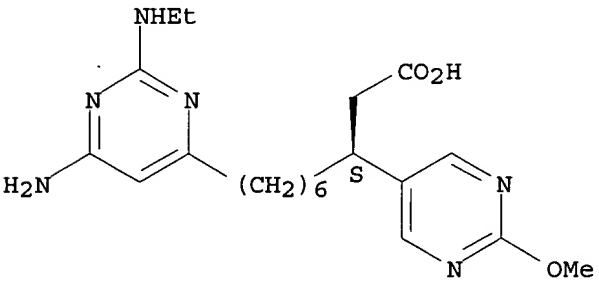


RN 351446-28-1 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

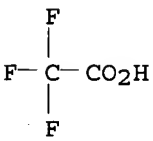
CRN 351446-27-0
CMF C20 H30 N6 O3

Absolute stereochemistry.



CM 2

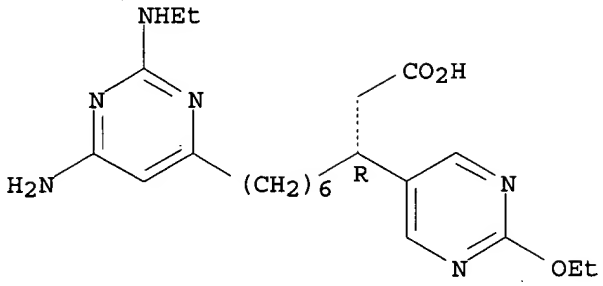
CRN 76-05-1
CMF C2 H F3 O2



RN 351446-29-2 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/ 400,992~~

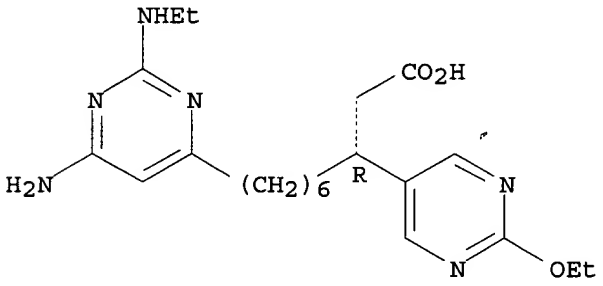


RN 351446-30-5 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

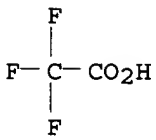
CRN 351446-29-2
CMF C21 H32 N6 O3

Absolute stereochemistry.



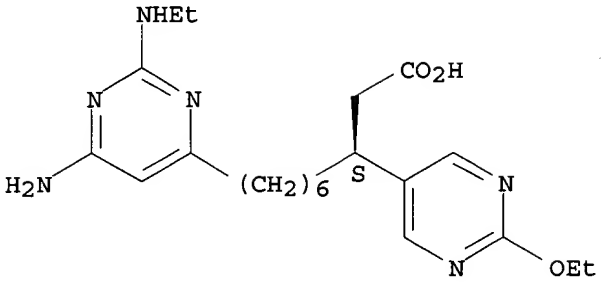
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-31-6 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

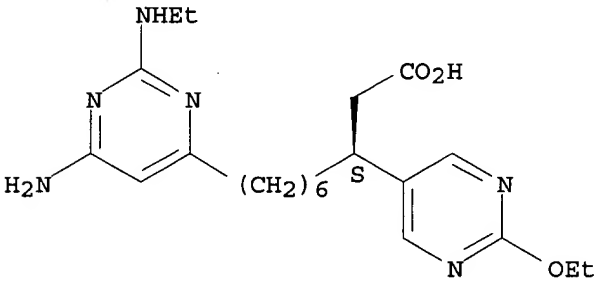


RN 351446-32-7 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

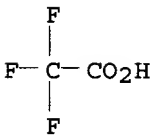
CRN 351446-31-6
CMF C21 H32 N6 O3

Absolute stereochemistry.



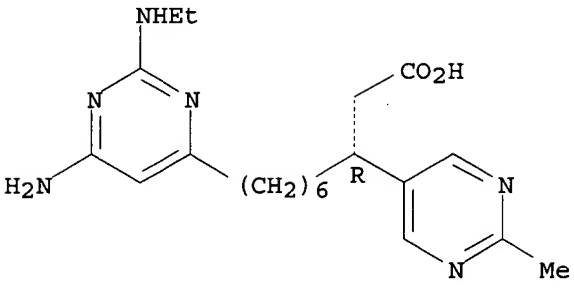
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-33-8 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

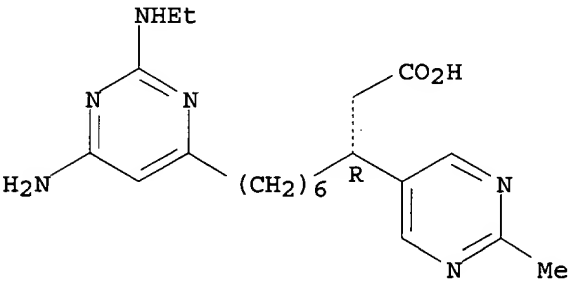


RN 351446-34-9 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

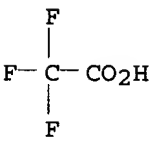
CRN 351446-33-8
CMF C20 H30 N6 O2

Absolute stereochemistry.



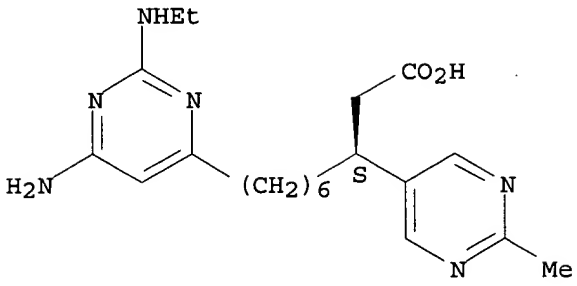
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-35-0 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

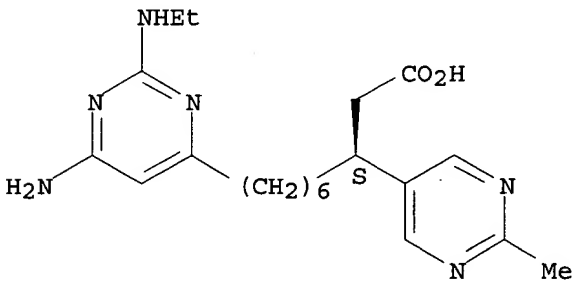


RN 351446-36-1 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

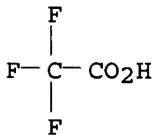
CRN 351446-35-0
CMF C20 H30 N6 O2

Absolute stereochemistry.



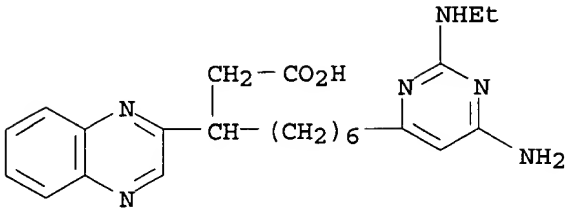
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-37-2 CAPLUS
CN 2-Quinoxalinepropanoic acid, .beta.-[6-[6-amino-2-(ethylamino)-4-pyrimidinyl]hexyl]- (9CI) (CA INDEX NAME)

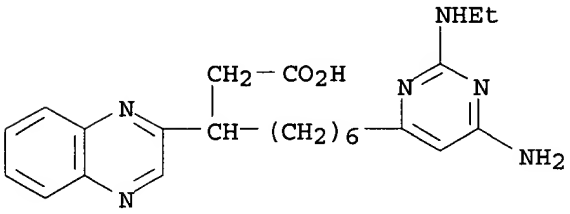
~~09/400,992~~



RN 351446-38-3 CAPLUS
CN 2-Quinoxalinepropanoic acid, .beta.-[6-[6-amino-2-(ethylamino)-4-pyrimidinyl]hexyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

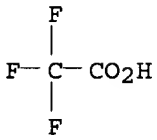
CM 1

CRN 351446-37-2
CMF C23 H30 N6 O2



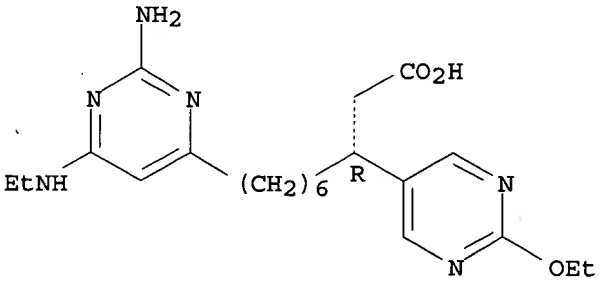
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-39-4 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-6-(ethylamino)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



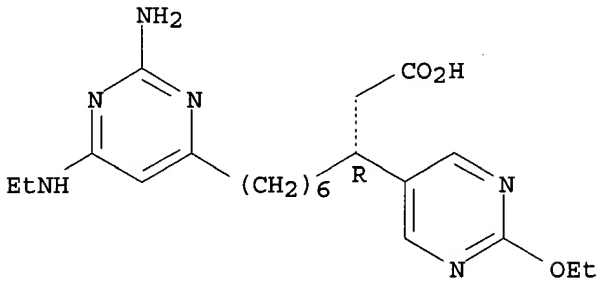
~~09/400,992~~

RN 351446-40-7 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-6-(ethylamino)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

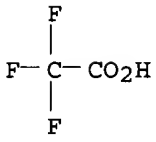
CRN 351446-39-4
CMF C21 H32 N6 O3

Absolute stereochemistry.



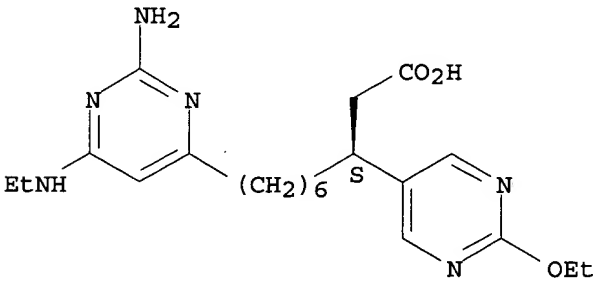
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-41-8 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-6-(ethylamino)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

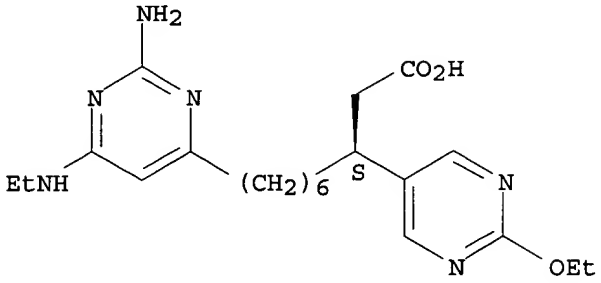


RN 351446-42-9 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-6-(ethylamino)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

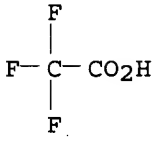
CRN 351446-41-8
CMF C21 H32 N6 O3

Absolute stereochemistry.



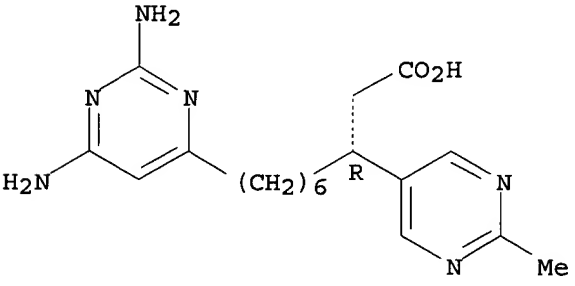
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-43-0 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2,6-diamino-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



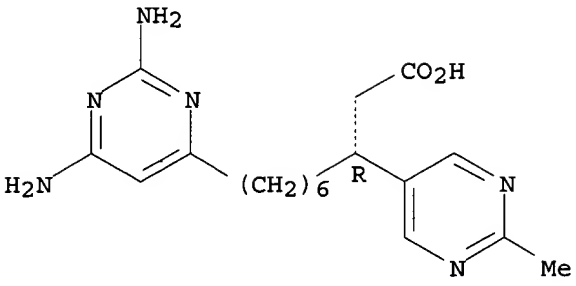
RN 351446-44-1 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2,6-diamino-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 351446-43-0
CMF C18 H26 N6 O2

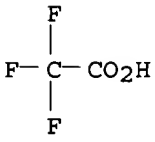
Absolute stereochemistry.

~~09/400,892~~



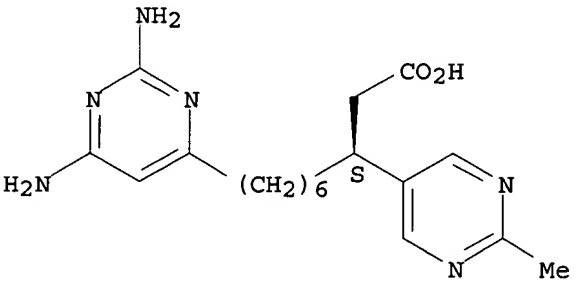
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-45-2 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2,6-diamino-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



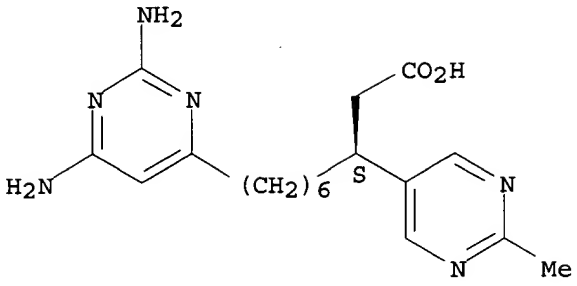
RN 351446-46-3 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2,6-diamino-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 351446-45-2
CMF C18 H26 N6 O2

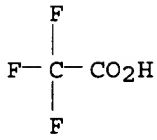
Absolute stereochemistry.

~~09/400,992~~



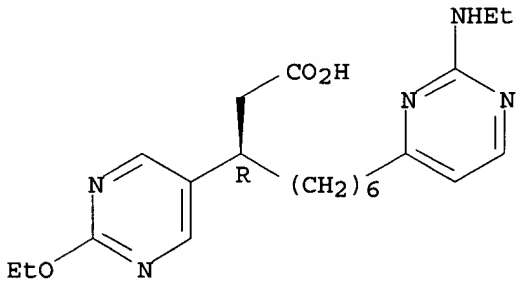
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-47-4 CAPLUS
CN 4-Pyrimidinenonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



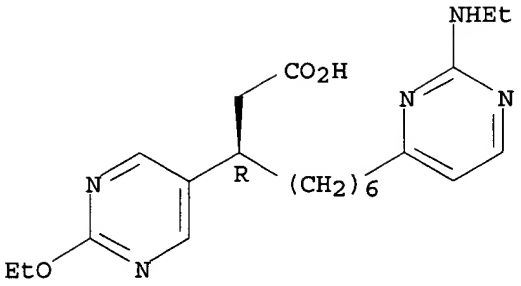
RN 351446-48-5 CAPLUS
CN 4-Pyrimidinenonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 351446-47-4
CMF C21 H31 N5 O3

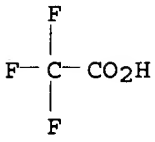
Absolute stereochemistry.

~~09/400,992~~



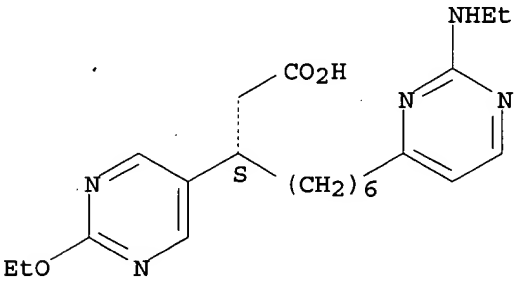
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 351446-49-6 CAPLUS
CN 4-Pyrimidinenonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

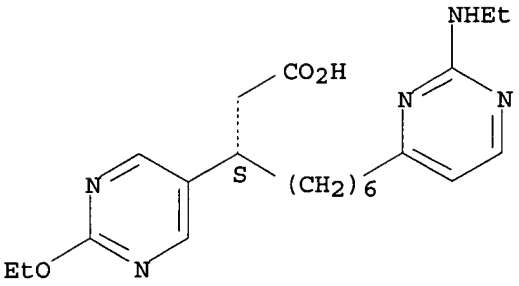


RN 351446-50-9 CAPLUS
CN 4-Pyrimidinenonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

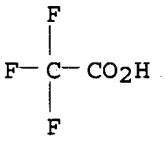
CRN 351446-49-6
CMF C21 H31 N5 O3

Absolute stereochemistry.

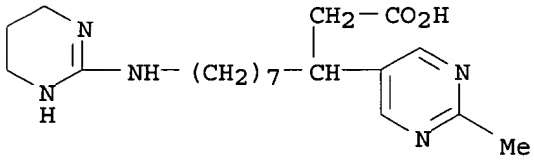


CM 2

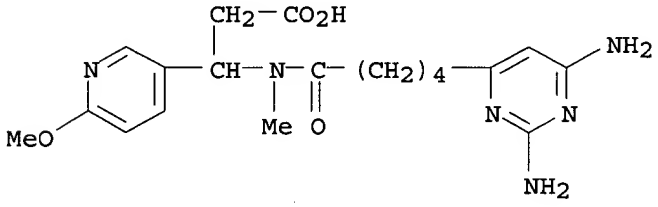
CRN 76-05-1
CMF C2 H F3 O2



RN 351446-56-5 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]- (9CI) (CA INDEX NAME)



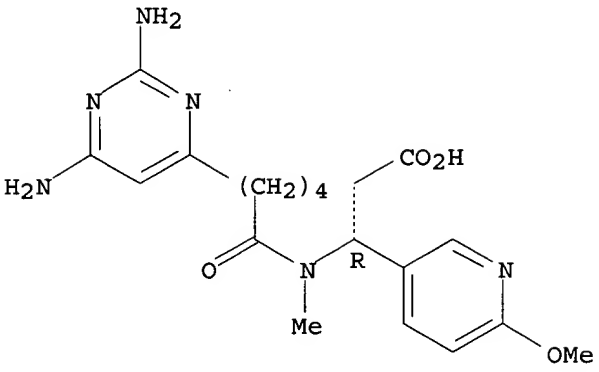
RN 351446-57-6 CAPLUS
CN 3-Pyridinepropanoic acid, .beta.-[[5-(2,6-diamino-4-pyrimidinyl)-1-oxopentyl]methylamino]-6-methoxy- (9CI) (CA INDEX NAME)



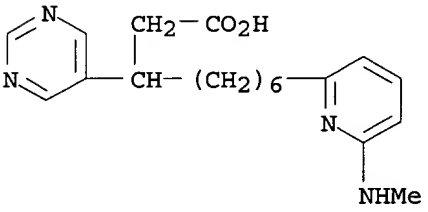
RN 351446-58-7 CAPLUS
CN 3-Pyridinepropanoic acid, .beta.-[[5-(2,6-diamino-4-pyrimidinyl)-1-oxopentyl]methylamino]-6-methoxy-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~

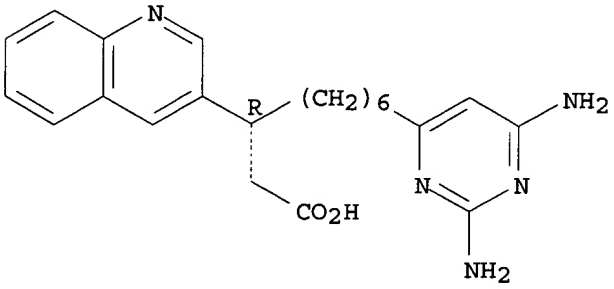


RN 351446-62-3 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-
(9CI) (CA INDEX NAME)



RN 351446-63-4 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-[6-(2,6-diamino-4-pyrimidinyl)hexyl]-,
(.beta.R)- (9CI) (CA INDEX NAME)

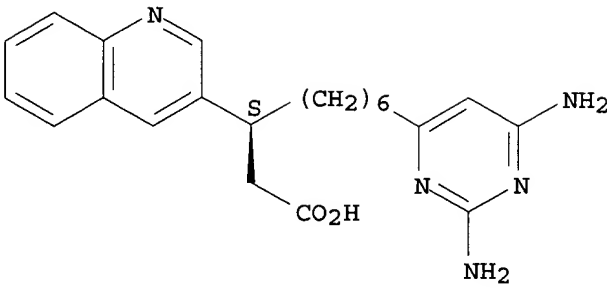
Absolute stereochemistry.



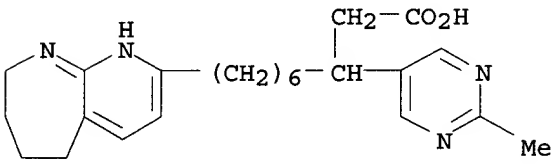
RN 351446-64-5 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-[6-(2,6-diamino-4-pyrimidinyl)hexyl]-,
(.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

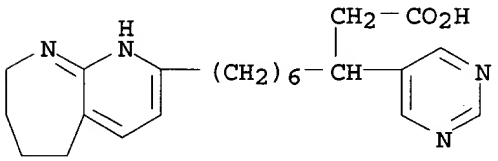
~~89/400,992~~



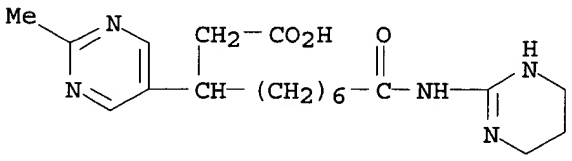
RN 351446-65-6 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 351446-66-7 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-5-pyrimidinyl- (9CI) (CA INDEX NAME)



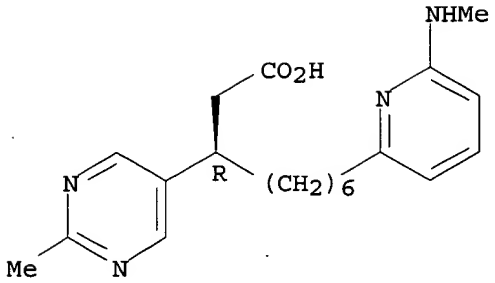
RN 351446-67-8 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-oxo-7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]- (9CI) (CA INDEX NAME)



RN 351446-68-9 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

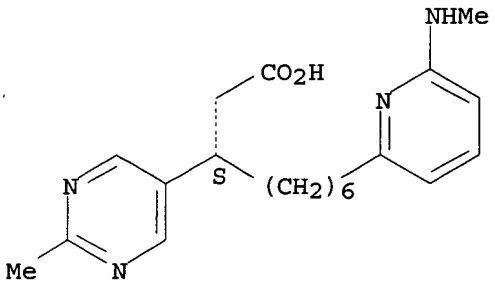
Absolute stereochemistry.

~~09/400,992~~



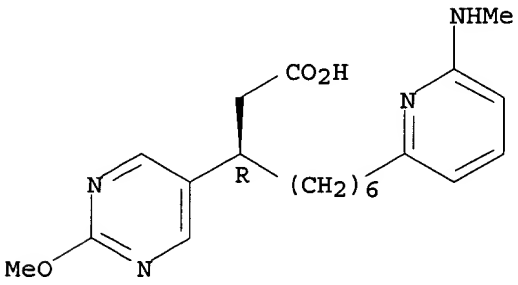
RN 351446-69-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



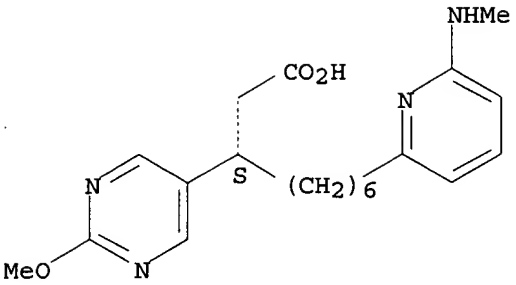
RN 351446-70-3 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methoxy-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



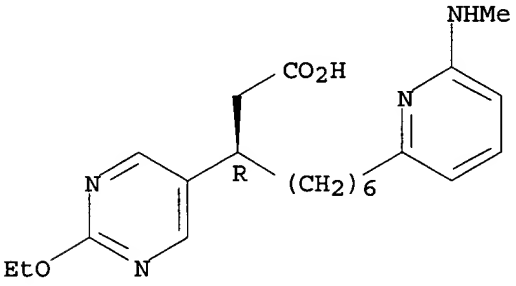
RN 351446-71-4 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methoxy-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



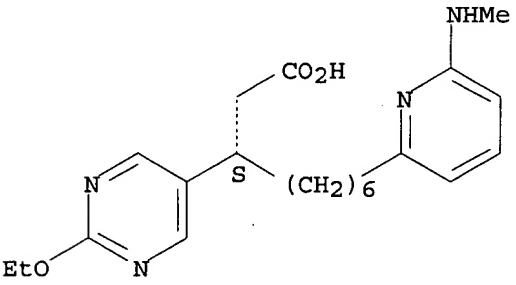
RN 351446-72-5 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351446-73-6 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

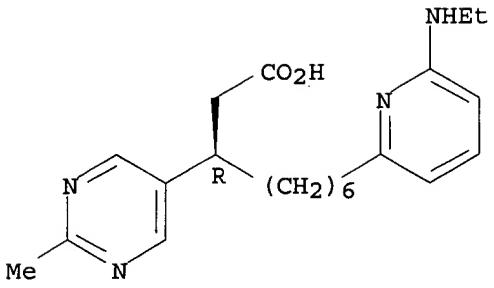
Absolute stereochemistry.



RN 351446-74-7 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-2-methyl-, (.beta.R)- (9CI) (CA INDEX NAME)

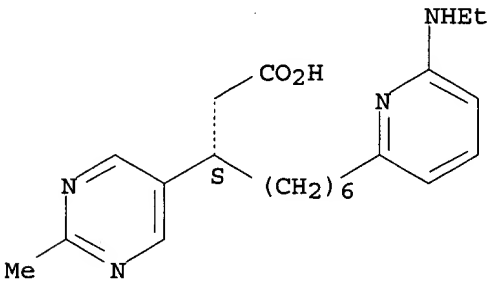
Absolute stereochemistry.

~~09/400,992~~



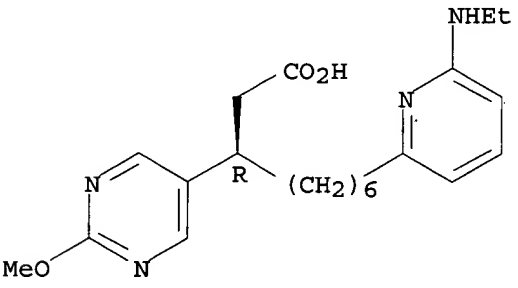
RN 351446-75-8 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-2-methyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351446-76-9 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-2-methoxy-, (.beta.R)- (9CI) (CA INDEX NAME)

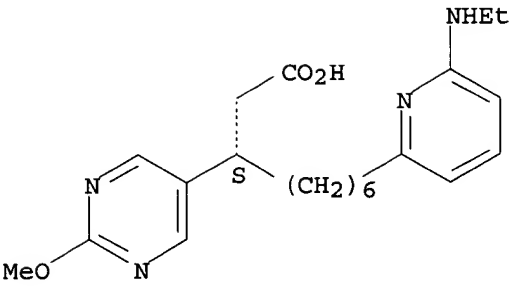
Absolute stereochemistry.



RN 351446-77-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-2-methoxy-, (.beta.S)- (9CI) (CA INDEX NAME)

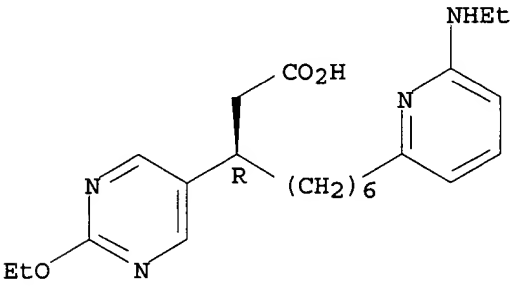
Absolute stereochemistry.

~~09/400,992~~



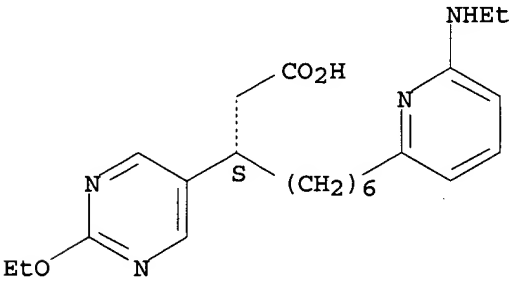
RN 351446-78-1 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

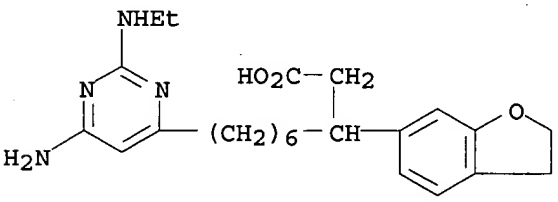


RN 351446-79-2 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-ethoxy-.beta.-[6-[6-(ethylamino)-2-pyridinyl]hexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

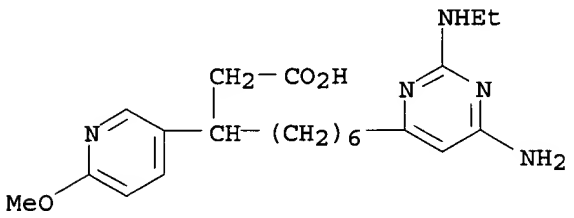
Absolute stereochemistry.



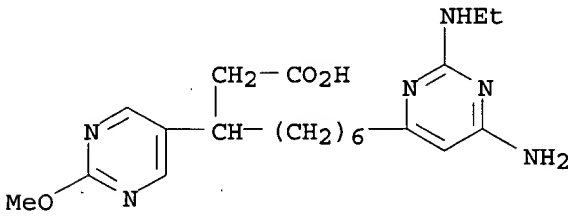
RN 351446-80-5 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2,3-dihydro-6-benzofuranyl)-2-(ethylamino)- (9CI) (CA INDEX NAME)



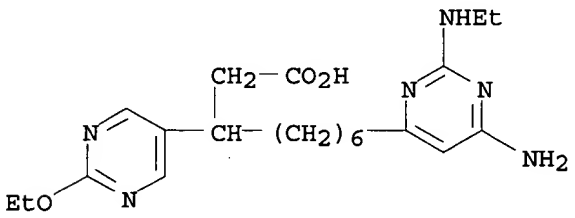
RN 351446-81-6 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



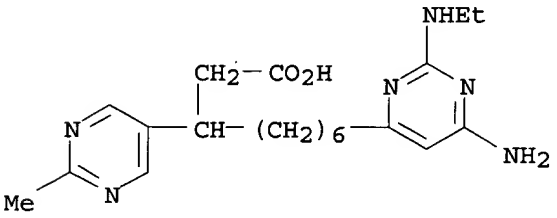
RN 351446-82-7 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methoxy-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 351446-85-0 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)- (9CI) (CA INDEX NAME)

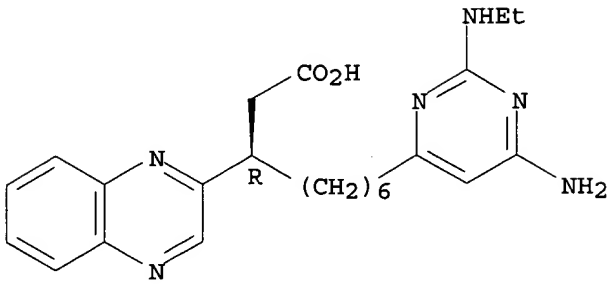


RN 351446-89-4 CAPLUS
CN 4-Pyrimidinenonanoic acid, 6-amino-2-(ethylamino)-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



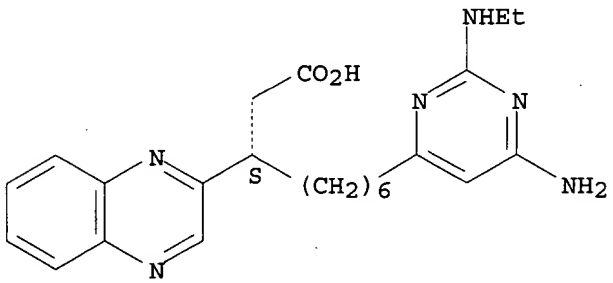
RN 351446-92-9 CAPLUS
CN 2-Quinoxalinepropanoic acid, .beta.-[6-[6-amino-2-(ethylamino)-4-pyrimidinyl]hexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

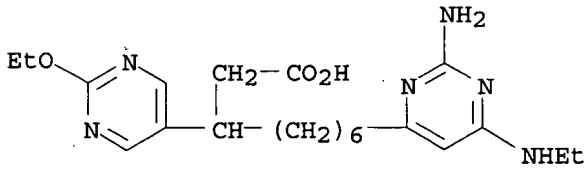


RN 351446-93-0 CAPLUS
CN 2-Quinoxalinepropanoic acid, .beta.-[6-[6-amino-2-(ethylamino)-4-pyrimidinyl]hexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

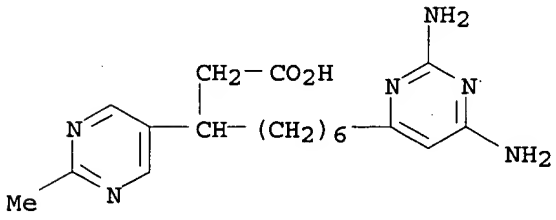
Absolute stereochemistry.



RN 351446-94-1 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2-amino-.beta.-(2-ethoxy-5-pyrimidinyl)-6-(ethylamino)- (9CI) (CA INDEX NAME)



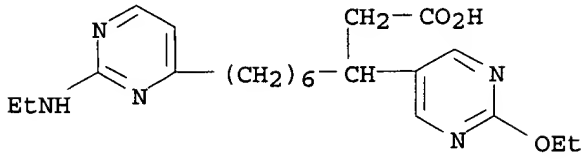
RN 351446-95-2 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2,6-diamino-.beta.-(2-methyl-5-pyrimidinyl)-(9CI) (CA INDEX NAME)



RN 351446-96-3 CAPLUS
CN 4-Pyrimidinenonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-2-(ethylamino)-

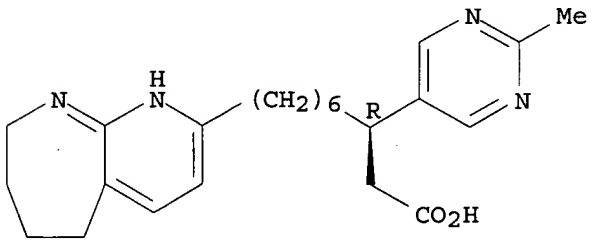
~~09/400,992~~

(9CI) (CA INDEX NAME)



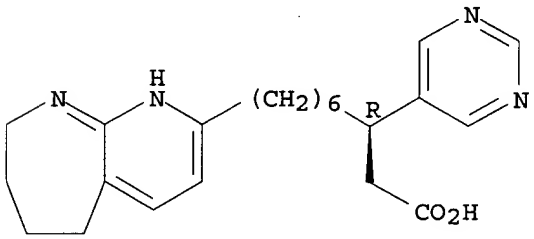
RN 351496-31-6 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



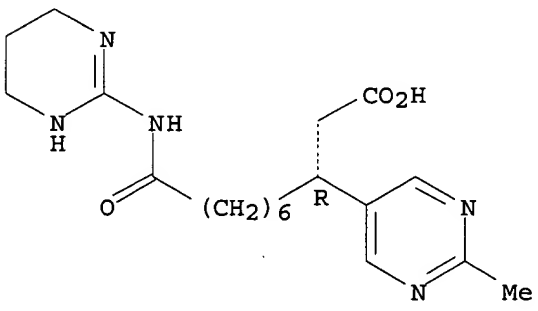
RN 351496-32-7 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 351496-33-8 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[7-oxo-7-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]heptyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

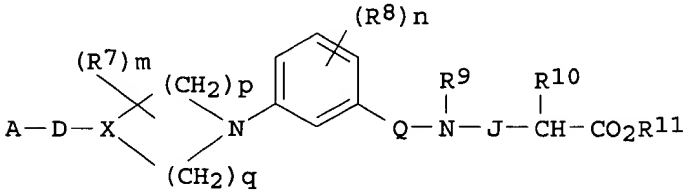


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:283934 CAPLUS
DOCUMENT NUMBER: 134:295835
TITLE: Preparation of m-substituted benzoic acid derivatives exhibiting **integrin** .alpha.v.beta.3 antagonism
INVENTOR(S): Ajito, Keiichi; Ishikawa, Minoru; Kubota, Dai; Murakami, Shoichi; Yamamoto, Mikio; Yahata, Naokazu; Fujishima, Kazuyuki; Oyama, Makoto
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027090	A1	20010419	WO 2000-JP7031	20001010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000075599	A5	20010423	AU 2000-75599	20001010
EP 1229024	A1	20020807	EP 2000-964758	20001010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-288487 A 19991008
WO 2000-JP7031 W 20001010
OTHER SOURCE(S): MARPAT 134:295835
GI



I

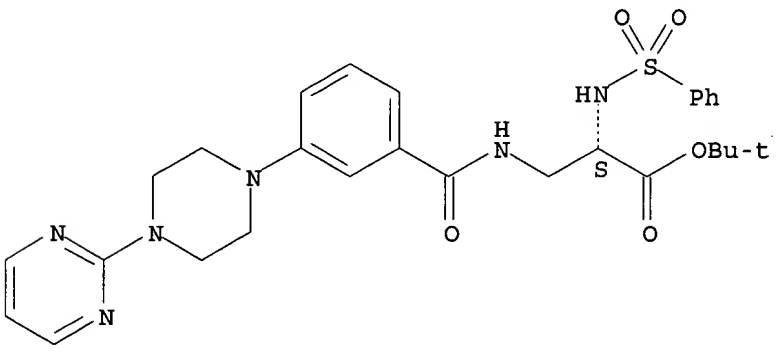
AB M-Substituted benzoic acid derivs. represented by general formula [I; A = (un)substituted H2NC(:NH), optionally substituted (un)satd. 5- to 7-membered ring heterocyclyl contg. 2 N atoms optionally condensed with other 5- to 7-membered ring carbocyclic or heterocyclic rin to form an (un)substituted bicyclic ring; D = single bond, (un)substituted NH; X = CH, N; R7, R8 = (un)substituted C1-6 alkyl or alkoxy, halo, NH2, NO2, cyano, OH, SH, C1-4 alkyl thio, phenylthio, O; Q = CO, CH2, C1-6 alkyl-CH; R9 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, or aralkyl; J = single

bond, (un)substituted C1-3 alkylene; R10 = H, (un)substituted HO, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, aralkyl, or NH2; R11 = H, (un)substituted aralkyl or C1-6 alkyl; m = 0-5; n = 0-4; p, q = 0-3], which improve **integrin** .alpha.v.beta.3 antagonism over **integrin** .alpha.11b.beta.3 antagonism and water soly., are prepd. These compds. also exhibit glycoprotein IIb/IIIa antagonism and cell adhesion-inhibitory and blood platelet aggregation-inhibitory activity. These derivs. are useful in the treatment or prevention of cardiovascular diseases, vascularization-related diseases, cerebrovascular diseases, cancers and metastases thereof, immunol. diseases, bone diseases, and so on. Thus, (2S)-(+)-Benzenesulfonylamino-3-[3-{4-(pyrimidin-2-yl)piperazin-1-yl}benzoylamino]propionic acid (prepn. given) was hydrogenated over 10% Pd/C in a mixt. of 1,4-dioxane, acetic acid, and 1 N aq. HCl under hydrogen atm. with stirring for 5 h to give (2S)-(+)-Benzenesulfonylamino-3-[3-{4-(1,4,5,6-tetrahydropyrimidin-2-yl)piperazin-1-yl}benzoylamino]propionic acid (II). II in vitro exhibited **integrin** .alpha.v.beta.3 antagonism and glycoprotein IIb/IIIa antagonism with IC50 of 1.3 and 2.0 nM, resp.

IT **334792-09-5P 334792-10-8P 334792-18-6P**
334792-19-7P 334792-27-7P 334792-28-8P
334792-39-1P 334792-42-6P 334792-48-2P
334792-50-6P 334792-61-9P 334792-63-1P
334792-69-7P 334792-74-4P 334792-83-5P
334792-85-7P 334792-94-8P 334792-96-0P
334792-98-2P 334792-99-3P 334793-00-9P
334793-02-1P 334793-04-3P 334793-06-5P
334793-08-7P 334793-10-1P 334793-12-3P
334793-14-5P 334793-17-8P 334793-22-5P
334793-24-7P 334793-29-2P 334793-31-6P
334793-36-1P 334793-38-3P 334793-44-1P
334793-47-4P 334793-53-2P 334793-55-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of m-substituted benzoic acid derivs. as **integrin** .alpha.v.beta.3 antagonists and therapeutics)

RN 334792-09-5 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

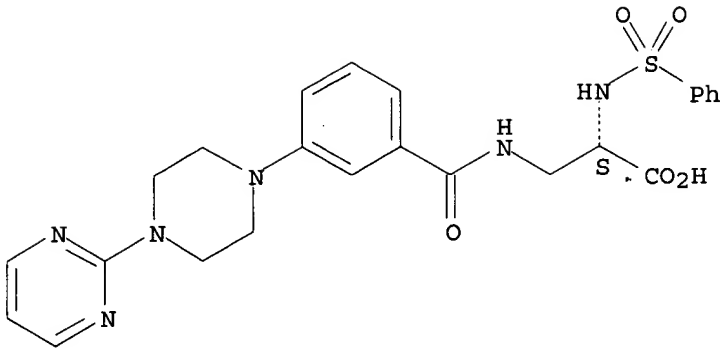
Absolute stereochemistry. Rotation (+).



RN 334792-10-8 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

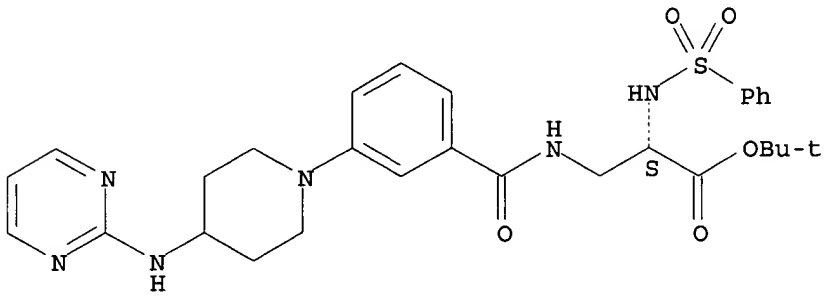
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



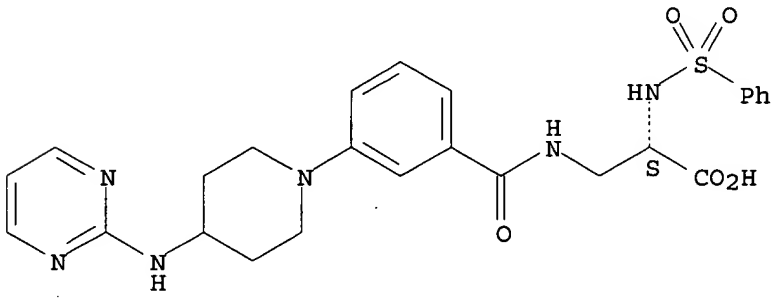
RN 334792-18-6 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334792-19-7 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

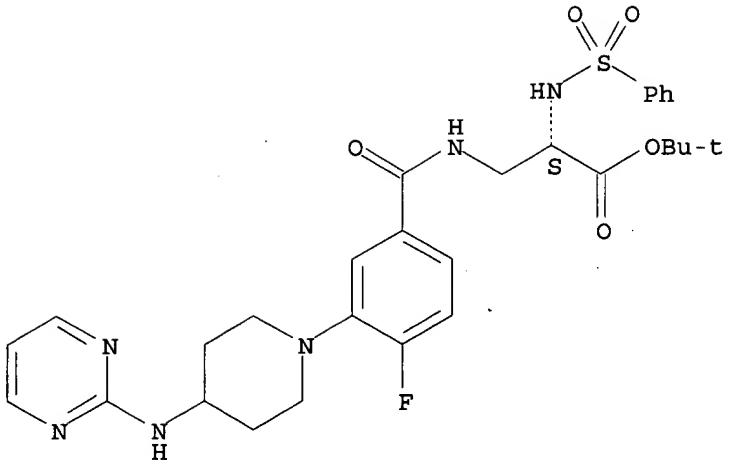
Absolute stereochemistry. Rotation (+).



RN 334792-27-7 CAPLUS
CN L-Alanine, 3-[[4-fluoro-3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

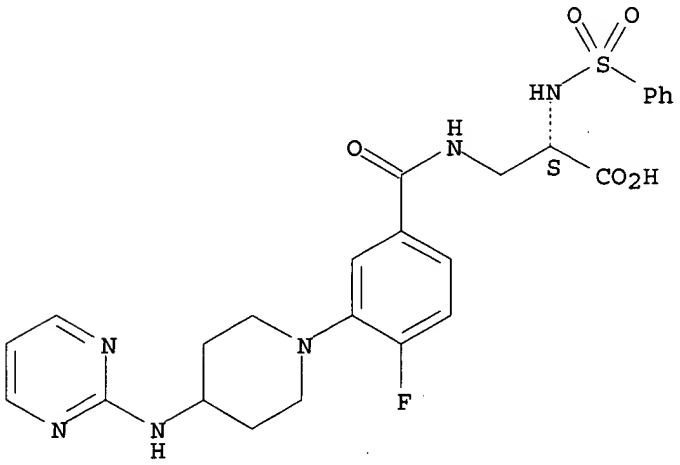
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



RN 334792-28-8 CAPLUS
CN L-Alanine, 3-[[4-fluoro-3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

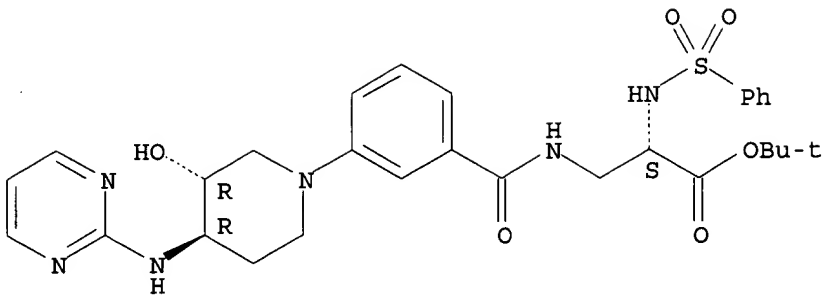
Absolute stereochemistry. Rotation (+).



RN 334792-39-1 CAPLUS
CN L-Alanine, 3-[[3-[(3R,4R)-3-hydroxy-4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

~~09/400,992~~

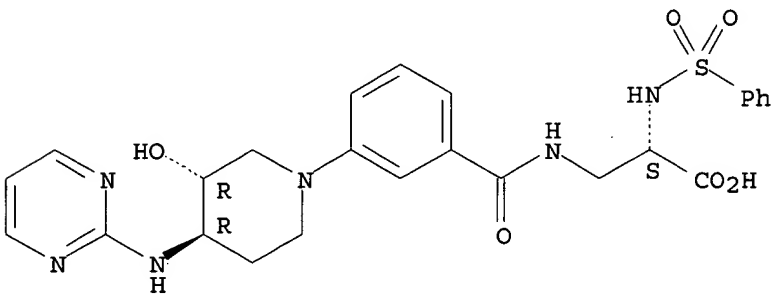


RN 334792-42-6 CAPLUS
CN L-Alanine, 3-[[3-[(3R,4R)-3-hydroxy-4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, tris(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

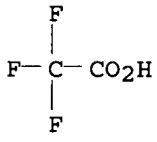
CRN 334792-41-5
CMF C25 H28 N6 O6 S

Absolute stereochemistry. Rotation (+).



CM 2

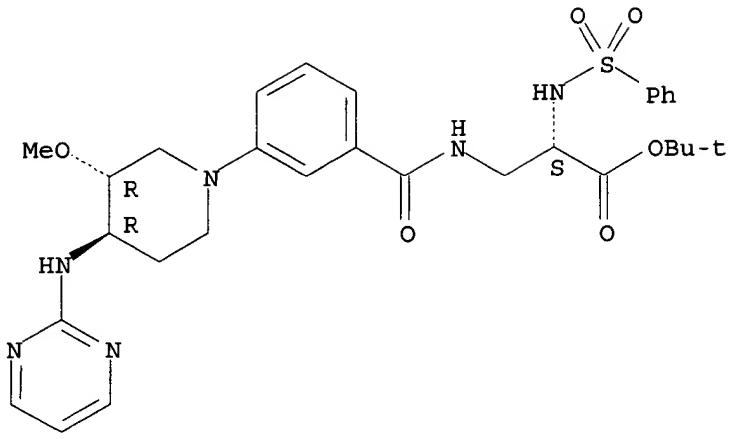
CRN 76-05-1
CMF C2 H F3 O2



RN 334792-48-2 CAPLUS
CN L-Alanine, 3-[[3-[(3R,4R)-3-methoxy-4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

~~09/400,992~~

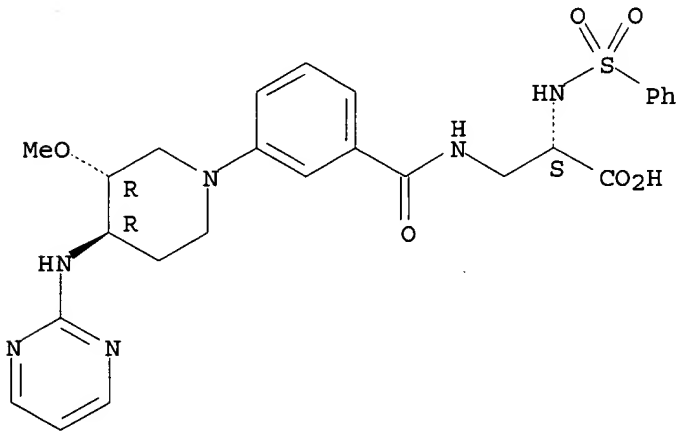


RN 334792-50-6 CAPLUS
CN L-Alanine, 3-[[3-[(3R,4R)-3-methoxy-4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

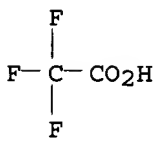
CRN 334792-49-3
CMF C26 H30 N6 O6 S

Absolute stereochemistry. Rotation (+).



CM 2

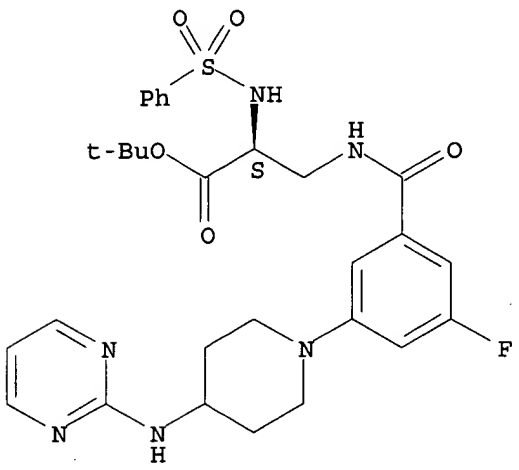
CRN 76-05-1
CMF C2 H F3 O2



RN 334792-61-9 CAPLUS
CN L-Alanine, 3-[[3-fluoro-5-[4-(2-pyrimidinylamino)-1-

piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

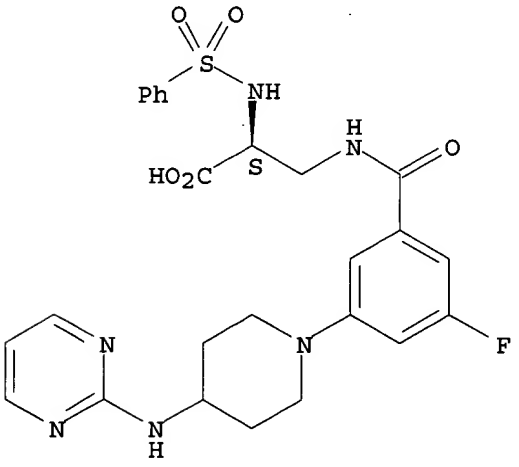


RN 334792-63-1 CAPLUS
CN L-Alanine, 3-[[3-fluoro-5-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

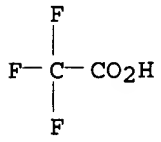
CRN 334792-62-0
CMF C25 H27 F N6 O5 S

Absolute stereochemistry. Rotation (+).



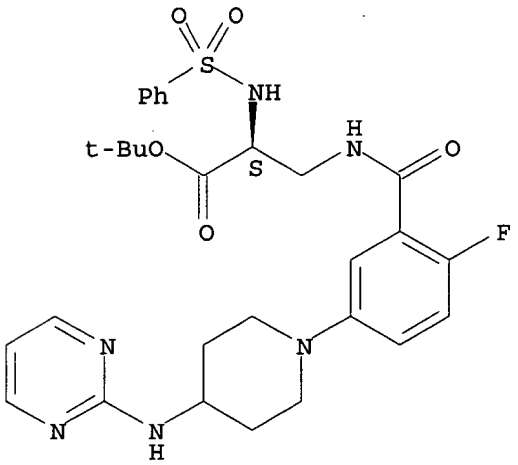
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334792-69-7 CAPLUS
CN L-Alanine, 3-[[2-fluoro-5-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

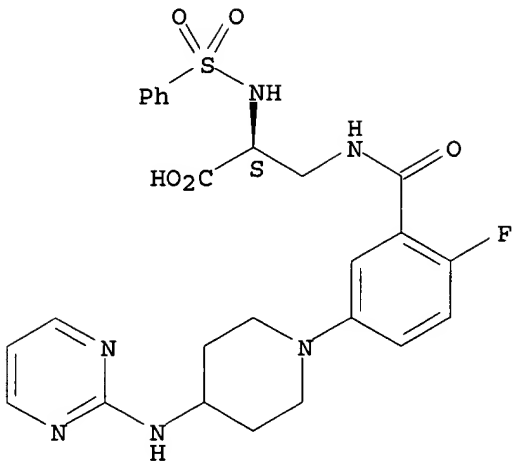


RN 334792-74-4 CAPLUS
CN L-Alanine, 3-[[2-fluoro-5-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

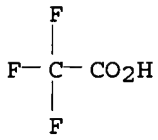
CRN 334792-73-3
CMF C25 H27 F N6 O5 S

Absolute stereochemistry. Rotation (+).



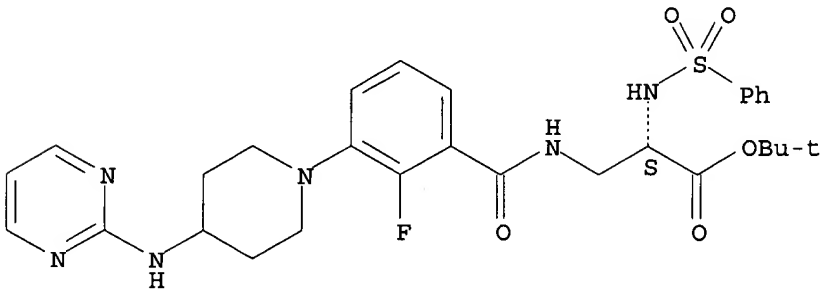
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334792-83-5 CAPLUS
CN L-Alanine, 3-[[2-fluoro-3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



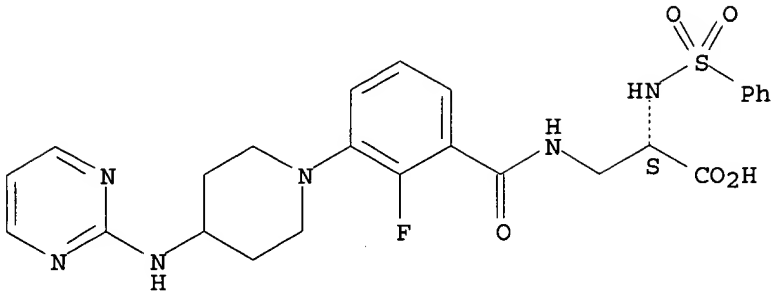
RN 334792-85-7 CAPLUS
CN L-Alanine, 3-[[2-fluoro-3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 334792-84-6
CMF C25 H27 F N6 O5 S

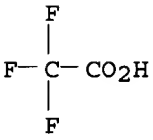
~~09/400,992~~

Absolute stereochemistry.



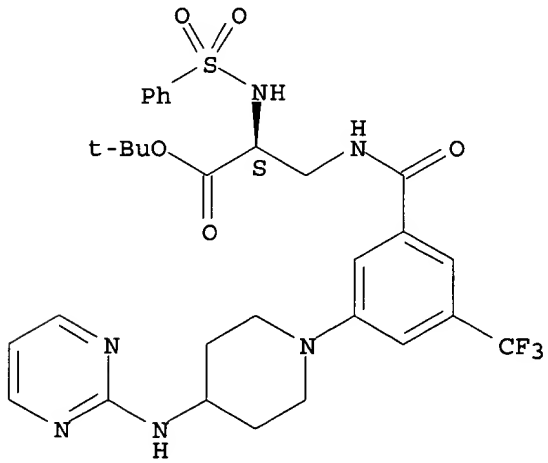
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334792-94-8 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]-5-(trifluoromethyl)benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

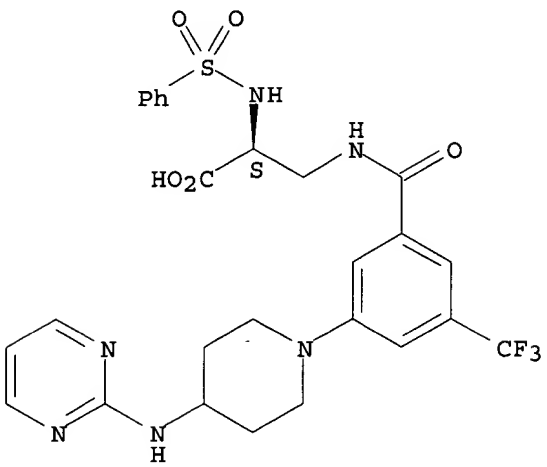


RN 334792-96-0 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]-5-(trifluoromethyl)benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

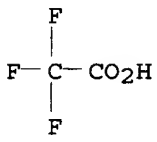
CRN 334792-95-9
CMF C26 H27 F3 N6 O5 S

Absolute stereochemistry.



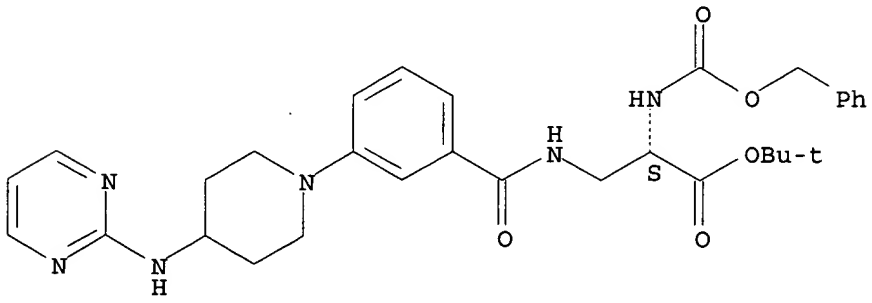
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334792-98-2 CAPLUS
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

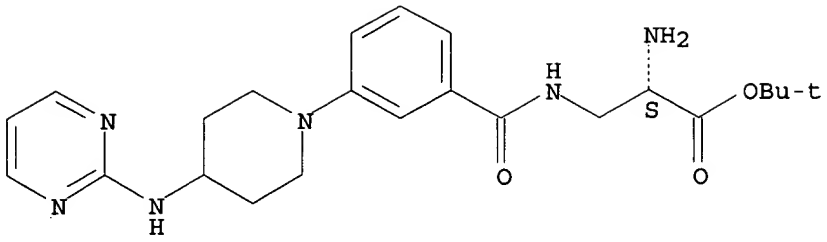
Absolute stereochemistry. Rotation (-).



RN 334792-99-3 CAPLUS
CN L-Alanine, 3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

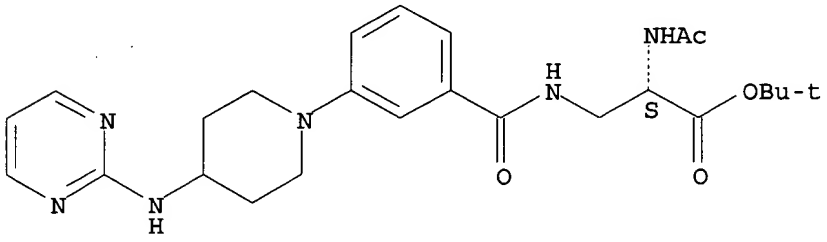
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



RN 334793-00-9 CAPLUS
CN L-Alanine, N-acetyl-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

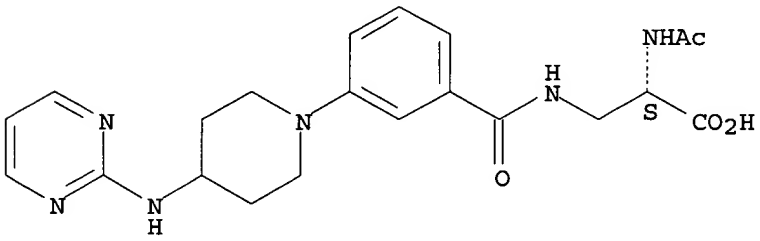


RN 334793-02-1 CAPLUS
CN L-Alanine, N-acetyl-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

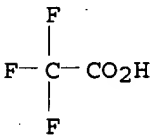
CRN 334793-01-0
CMF C21 H26 N6 O4

Absolute stereochemistry. Rotation (+).



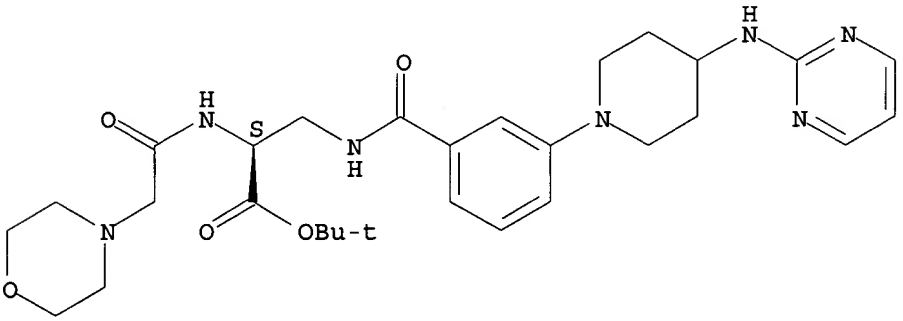
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334793-04-3 CAPLUS
CN L-Alanine, N-(4-morpholinylacetyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

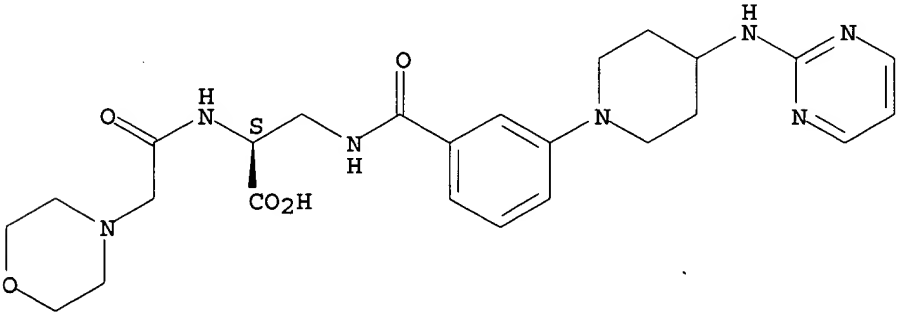


RN 334793-06-5 CAPLUS
CN L-Alanine, N-(4-morpholinylacetyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 334793-05-4
CMF C25 H33 N7 O5

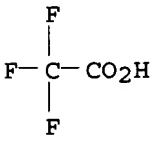
Absolute stereochemistry. Rotation (+).



CM 2

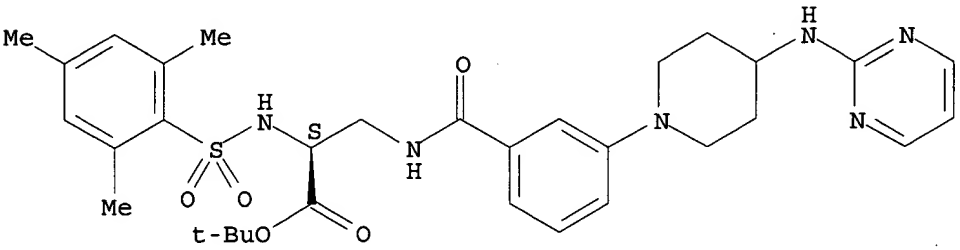
CRN 76-05-1
CMF C2 H F3 O2

~~09/400,992~~



RN 334793-08-7 CAPLUS
CN L-Alanine, 3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

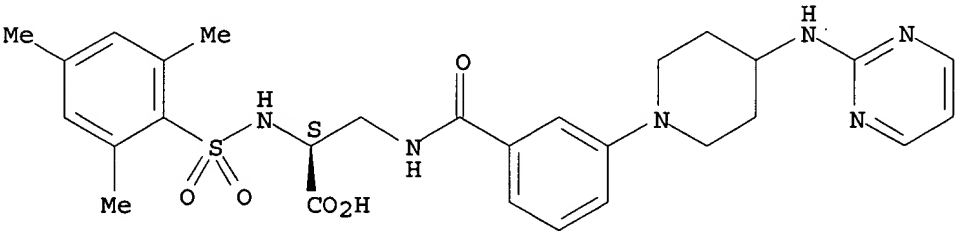


RN 334793-10-1 CAPLUS
CN L-Alanine, 3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

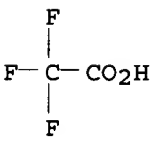
CRN 334793-09-8
CMF C28 H34 N6 O5 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 76-05-1
CMF C2 H F3 O2

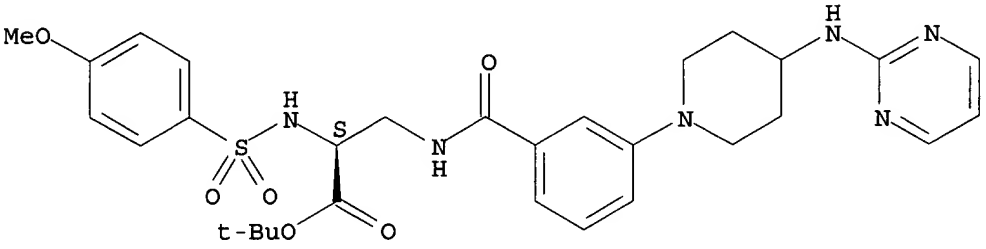


RN 334793-12-3 CAPLUS

~~09/400,992~~

CN L-Alanine, N-[(4-methoxyphenyl)sulfonyl]-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

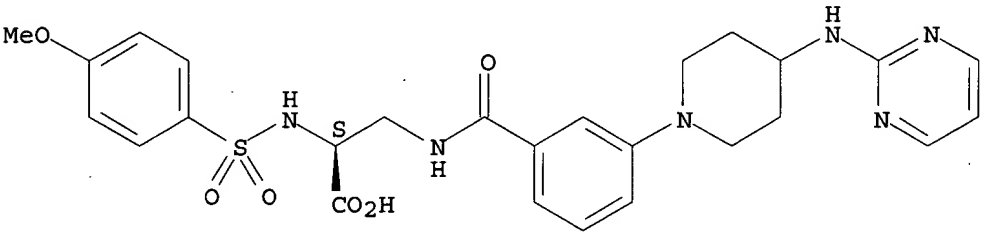


RN 334793-14-5 CAPLUS
CN L-Alanine, N-[(4-methoxyphenyl)sulfonyl]-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

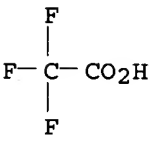
CRN 334793-13-4
CMF C26 H30 N6 O6 S

Absolute stereochemistry. Rotation (+).



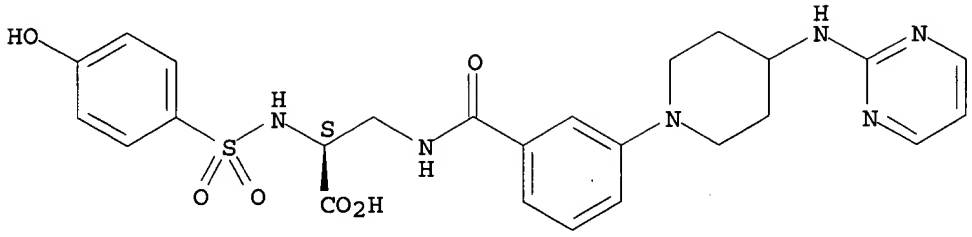
CM 2

CRN 76-05-1
CMF C2 H F3 O2



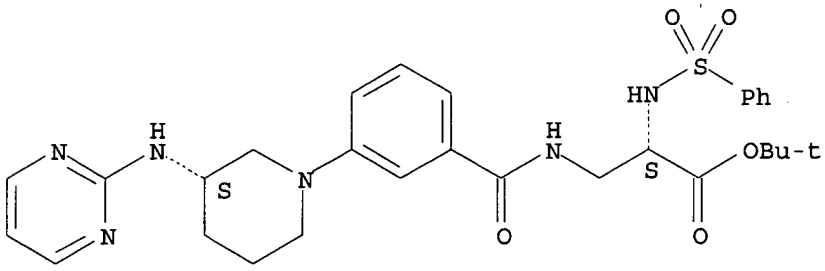
RN 334793-17-8 CAPLUS
CN L-Alanine, N-[(4-hydroxyphenyl)sulfonyl]-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334793-22-5 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

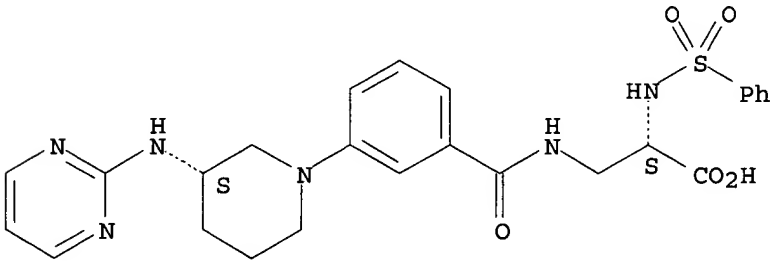


RN 334793-24-7 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

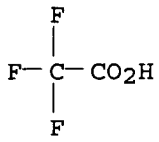
CRN 334793-23-6
CMF C25 H28 N6 O5 S

Absolute stereochemistry. Rotation (+).



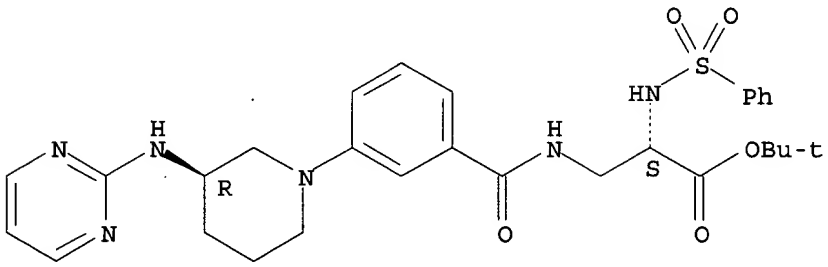
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334793-29-2 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

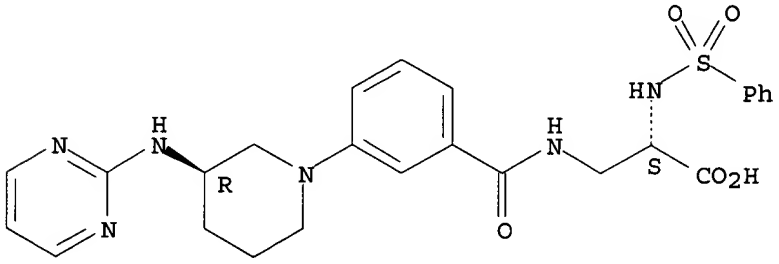


RN 334793-31-6 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

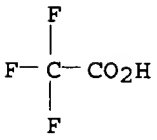
CRN 334793-30-5
CMF C25 H28 N6 O5 S

Absolute stereochemistry. Rotation (+).



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334793-36-1 CAPLUS

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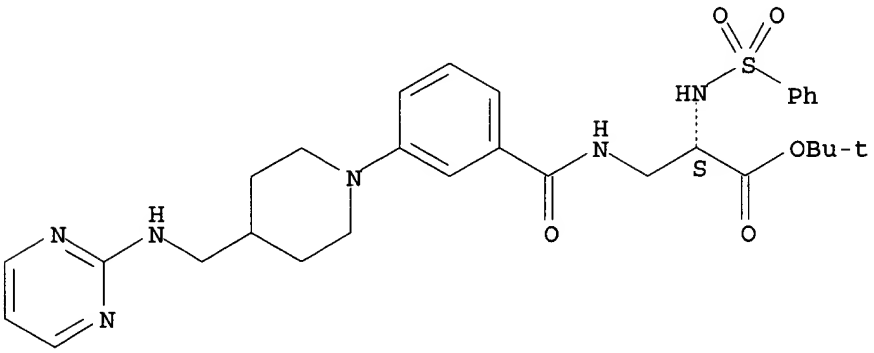
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-[(2-pyrimidinylamino)methyl]-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

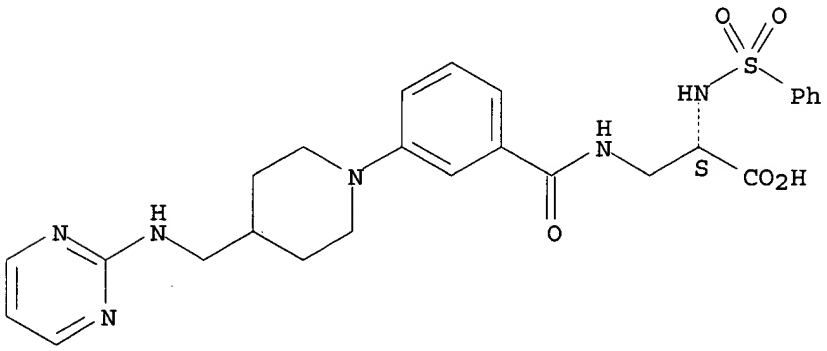


RN 334793-38-3 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-[(2-pyrimidinylamino)methyl]-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

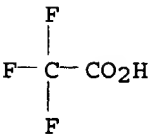
CRN 334793-37-2
CMF C26 H30 N6 O5 S

Absolute stereochemistry. Rotation (+).



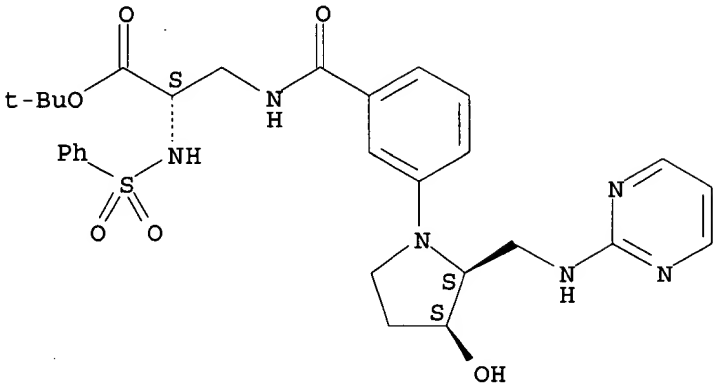
CM 2

CRN 76-05-1
CMF C2 H F3 O2



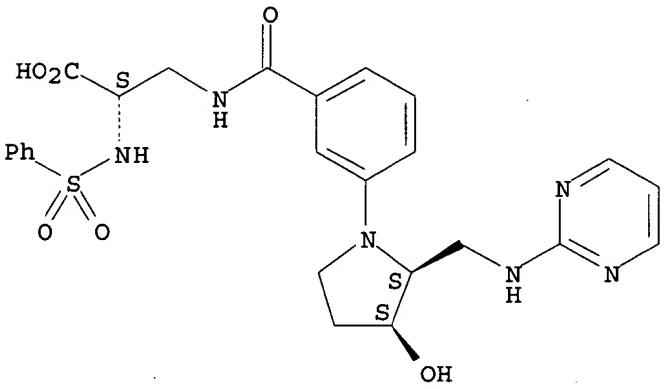
RN 334793-44-1 CAPLUS
CN L-Alanine, 3-[[3-[(2S,3S)-3-hydroxy-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



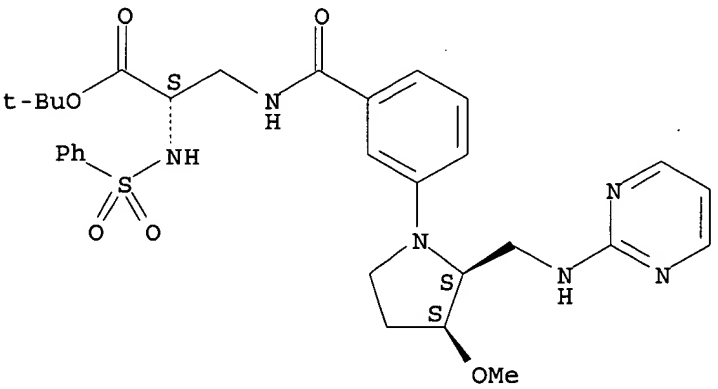
RN 334793-47-4 CAPLUS
CN L-Alanine, 3-[[3-[(2S,3S)-3-hydroxy-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334793-53-2 CAPLUS
CN L-Alanine, 3-[[3-[(2S,3S)-3-methoxy-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

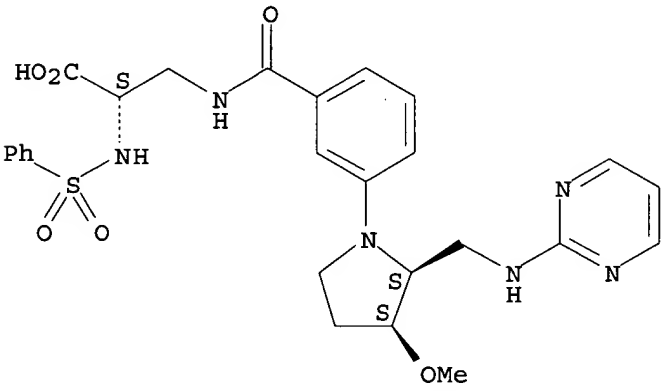


RN 334793-55-4 CAPLUS
CN L-Alanine, 3-[[3-[(2S,3S)-3-methoxy-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

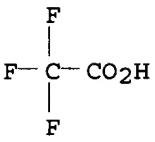
CRN 334793-54-3
CMF C26 H30 N6 O6 S

Absolute stereochemistry. Rotation (-).



CM 2

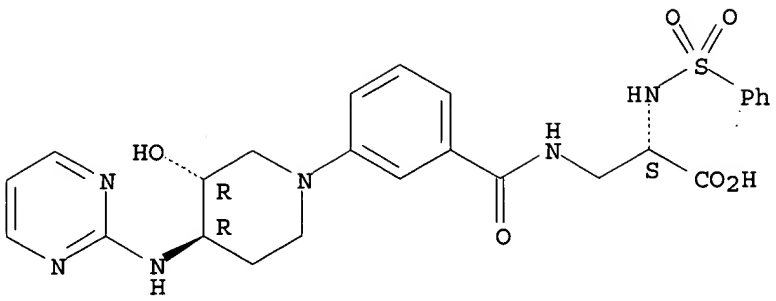
CRN 76-05-1
CMF C2 H F3 O2



IT **334792-41-5P 334792-49-3P 334792-62-0P**
334792-73-3P 334792-84-6P 334792-95-9P
334793-01-0P 334793-05-4P 334793-09-8P
334793-13-4P 334793-23-6P 334793-30-5P
334793-54-3P 334793-58-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of m-substituted benzoic acid derivs. as **integrin** .alpha.v.beta.3 antagonists and therapeutics)
RN 334792-41-5 CAPLUS
CN L-Alanine, 3-[[3-[(3R,4R)-3-hydroxy-4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

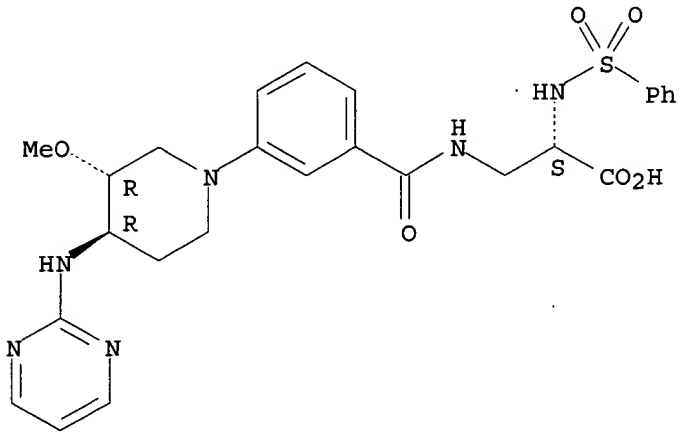
Absolute stereochemistry. Rotation (+).

~~09/400,982~~



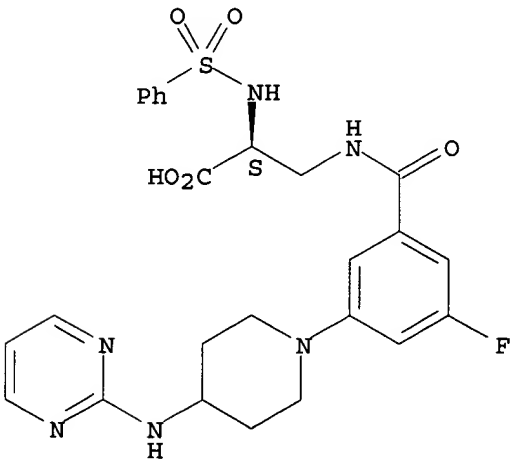
RN 334792-49-3 CAPLUS
CN L-Alanine, 3-[[3-[(3R,4R)-3-methoxy-4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334792-62-0 CAPLUS
CN L-Alanine, 3-[[3-fluoro-5-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

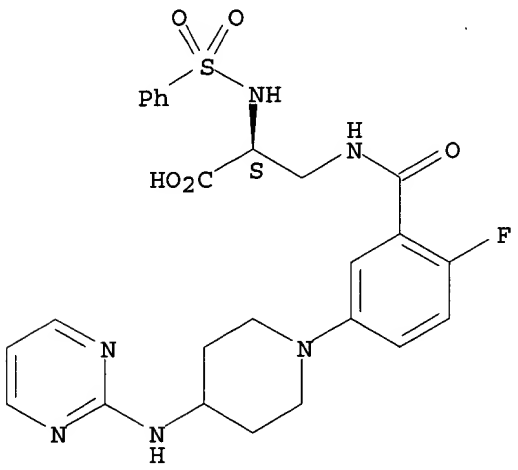


RN 334792-73-3 CAPLUS

~~09/400,992~~

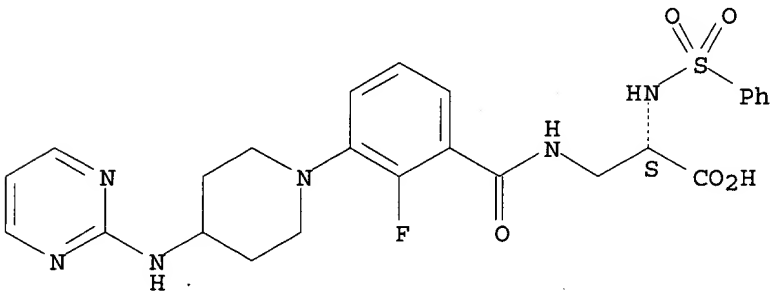
CN L-Alanine, 3-[[2-fluoro-5-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



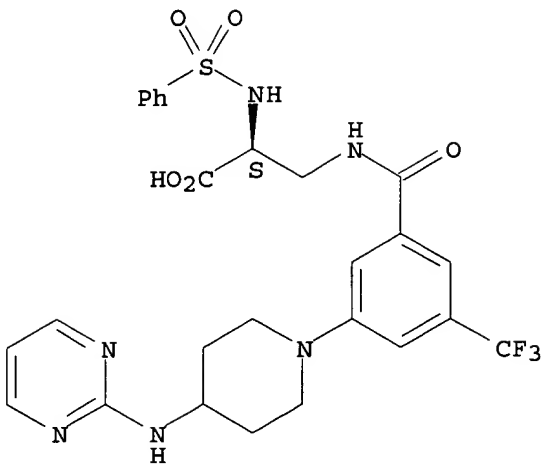
RN 334792-84-6 CAPLUS
CN L-Alanine, 3-[[2-fluoro-3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



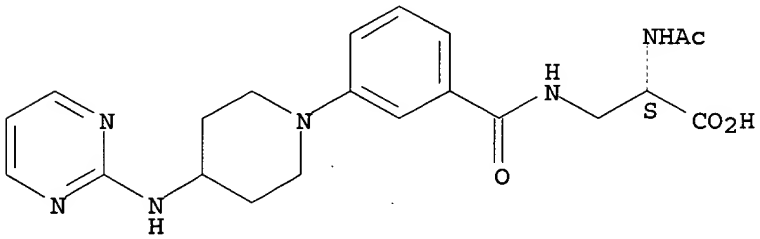
RN 334792-95-9 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]-5-(trifluoromethyl)benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



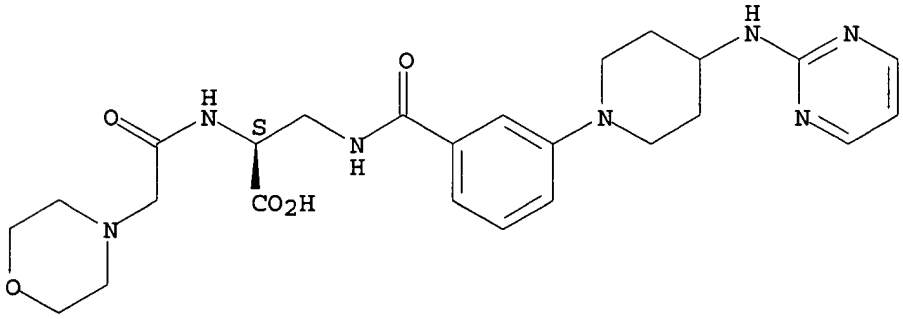
RN 334793-01-0 CAPLUS
CN L-Alanine, N-acetyl-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334793-05-4 CAPLUS
CN L-Alanine, N-(4-morpholinylacetyl)-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334793-09-8 CAPLUS
CN L-Alanine, 3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

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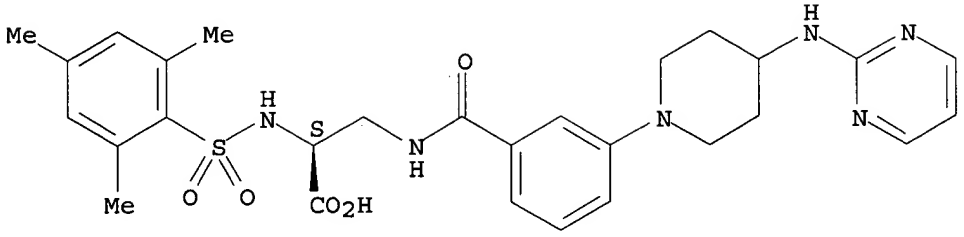
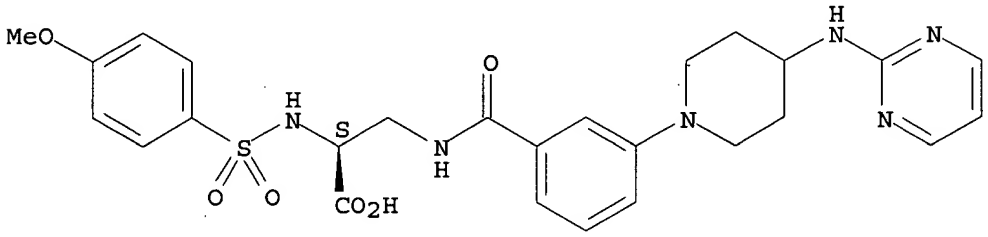


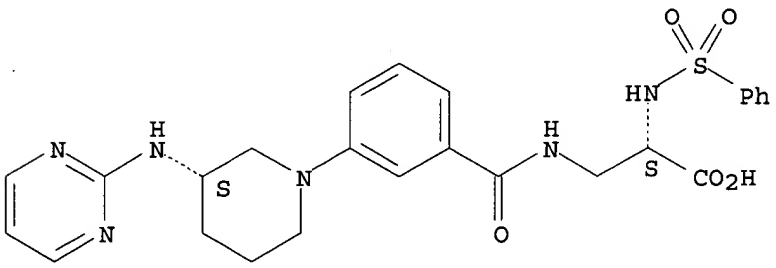
RN 334793-13-4 CAPLUS
CN L-Alanine, N-[(4-methoxyphenyl)sulfonyl]-3-[[3-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



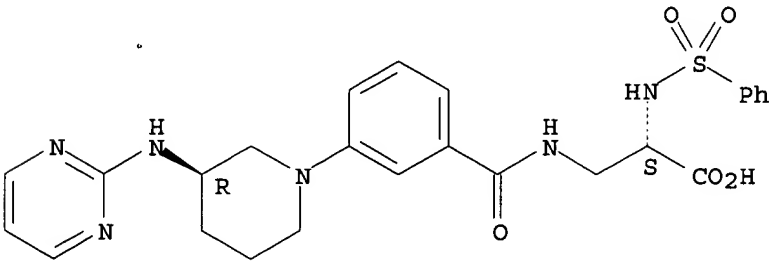
RN 334793-23-6 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334793-30-5 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

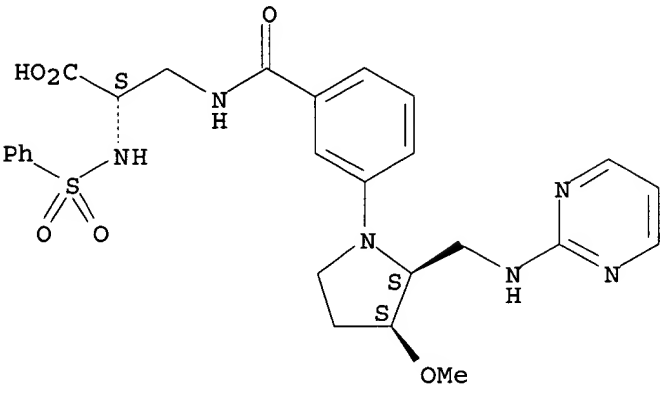


RN 334793-54-3 CAPLUS
CN L-Alanine, 3-[[3-[(2S,3S)-3-methoxy-2-[(2-pyrimidinylamino)methyl]-1-

~~09/400,992~~

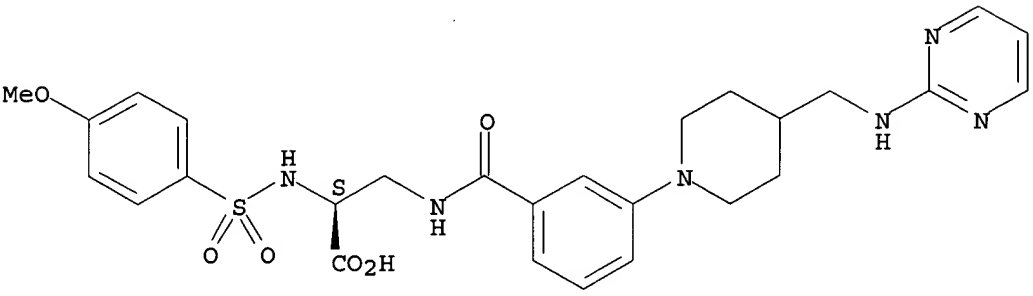
pyrrolidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 334793-58-7 CAPLUS
CN L-Alanine, N-[(4-methoxyphenyl)sulfonyl]-3-[[3-[4-[(2-pyrimidinylamino)methyl]-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:283926 CAPLUS
DOCUMENT NUMBER: 134:295833
TITLE: Preparation of 3-aminopiperidine derivatives as **integrin** .alpha.v.beta.3 antagonists
INVENTOR(S): Ishikawa, Minoru; Kubota, Dai; Hiraiwa, Yukiko; Tsushima, Masaki; Yamamoto, Mikio; Yahata, Naokazu; Kuroda, Chizuko; Abe, Mitsuhiro; Fujishima, Kazuyuki; Murakami, Shoichi; Ajito, Keiichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027082	A1	20010419	WO 2000-JP7033	20001010

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

09/400,992

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000075601 A5 20010423 AU 2000-75601 20001010

EP 1227083 A1 20020731 EP 2000-964760 20001010

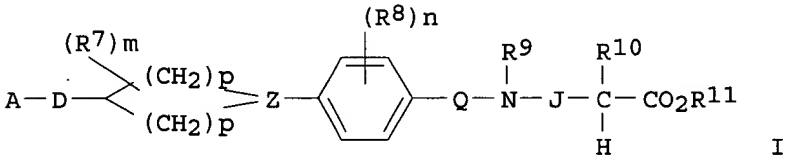
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: JP 1999-288904 A 19991008

WO 2000-JP7033 W 20001010

OTHER SOURCE(S): MARPAT 134:295833

GI



I

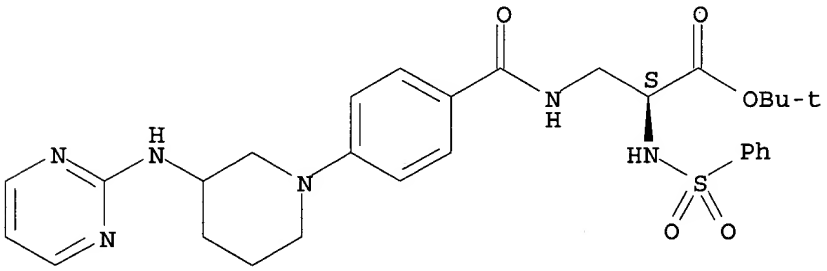
AB Compds. represented by general formula [I; A = (un)substituted C(:NH)NH2, C(:CH2)NH2, or heterocyclic group contg. at least one nitrogen atom; D = (un)substituted NH, O, S, or NHCH2; Z = CH, N; R7, R8 = (un)substituted C1-6 alkyl or alkoxy, halo, NH2, NO2, OH, O; Q = CO, CH2, C1-6 alkyl-CH, CHOH, (C1-6 alkoxy)-CH; R9 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, or aralkyl; J = single bond, (un)substituted C1-3 alkylene; R10 = H, OH, C1-6 alkoxy, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, aralkyl, or NH2; R11 = H, C1-6 optionally substituted by 1 or 2 Ph groups; m = 0-5; n = 0-4; p = 3,4; q = 0-3], wherein basic groups are attached to the 3-position of piperidine ring either directly or via various groups, are prepd. These compds. are useful for treating **integrin** .alpha.v.beta.3-mediated diseases or diseases for which cell adhesion-inhibitory, GP IIb/IIIa antagonism and/or blood platelet aggregation-inhibitory activity is effective and in particular are useful in treating or preventing cardiovascular diseases, diseases in assocn. with angiogenesis, cerebrovascular diseases, cancer and metastasis thereof, immune diseases, and bone diseases. Thus, 3-fluoro-4-[(3S)-3-(pyrimidin-2-ylamino)piperidin-1-yl]benzoic acid was condensed with (2S)-N-benzenesulfonyl-2,3-diaminopropanoic acid using 1-hydroxybenzotriazole, N-methylmorpholine, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMF at room temp. for 10 h to give (2S)-2-(benzenesulfonylamino)-3-[3-fluoro-4-[(3S)-3-(pyrimidin-2-ylamino)piperidin-1-yl]benzoylamino]propanoic acid tert-Bu ester which was treated with CF3CO2H in CH2Cl2 at room temp. for 20 h to give (2S)-2-(benzenesulfonylamino)-3-[3-fluoro-4-[(3S)-3-(pyrimidin-2-ylamino)piperidin-1-yl]benzoylamino]propanoic acid trifluoroacetate. The latter compd. was hydrogenated over 10% Pd-C in aq. dioxane at room temp. for 4 h to give, after chromatog. purifn., (2S)-2-(benzenesulfonylamino)-3-[3-fluoro-4-[(3S)-3-(1,4,5,6-tetrahydropyrimidin-2-ylamino)piperidin-1-yl]benzoylamino]propanoic acid, which.

IT **334617-98-0P 334618-01-8P 334618-02-9P 334618-16-5P 334618-18-7P 334618-29-0P 334618-31-4P 334618-32-5P 334618-36-9P 334618-39-2P 334618-41-6P 334618-43-8P**

334618-47-2P 334618-55-2P 334618-57-4P
334618-58-5P 334618-67-6P 334618-69-8P
334618-70-1P 334618-80-3P 334618-82-5P
334618-83-6P 334619-04-4P 334619-06-6P
334619-07-7P 334619-18-0P 334619-20-4P
334619-21-5P 334619-39-5P 334619-41-9P
334619-42-0P 334619-53-3P 334619-55-5P
334619-56-6P 334619-61-3P 334619-63-5P
334619-67-9P 334619-73-7P 334619-74-8P
334619-78-2P 334619-80-6P 334619-81-7P
334619-85-1P 334619-87-3P 334619-88-4P
334619-92-0P 334619-94-2P 334619-95-3P
334619-99-7P 334620-01-8P 334620-06-3P
334620-09-6P 334620-12-1P 334620-24-5P
334620-27-8P 334620-28-9P 334620-65-4P
334620-69-8P 334620-70-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 3-aminopiperidine derivs. as **integrin** .alpha.v.beta.3 antagonists for preventives or therapeutics)

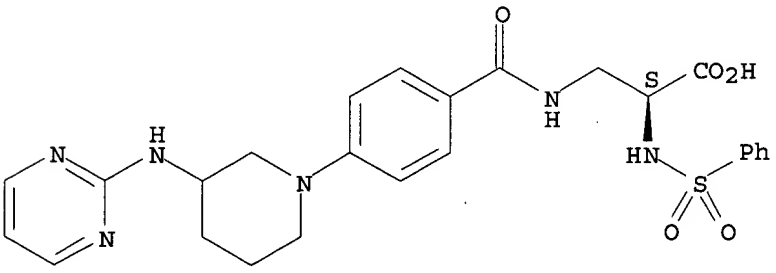
RN 334617-98-0 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334618-01-8 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

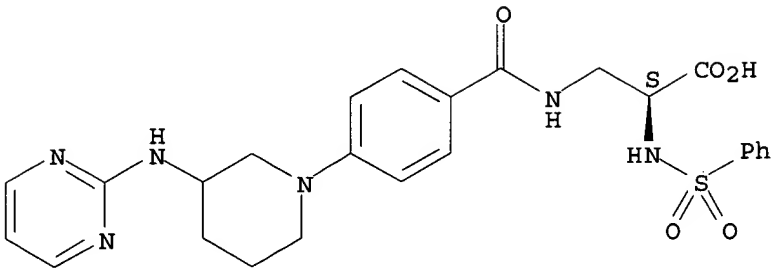


RN 334618-02-9 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

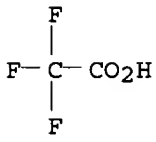
CRN 334618-01-8
CMF C25 H28 N6 O5 S

Absolute stereochemistry.



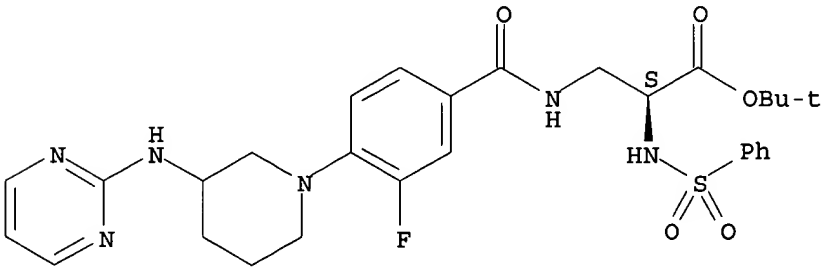
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334618-16-5 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

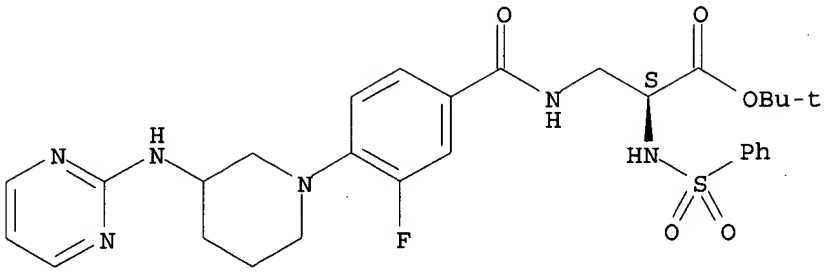


RN 334618-18-7 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

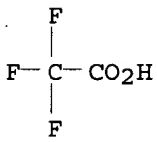
CRN 334618-16-5
CMF C29 H35 F N6 O5 S

Absolute stereochemistry.



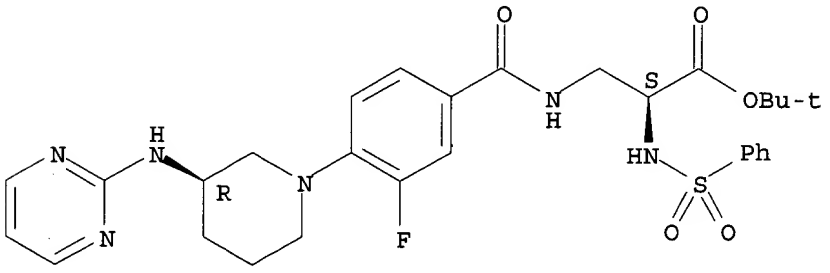
CM 2

CRN 76-05-1
CMF C2 H F3 O2



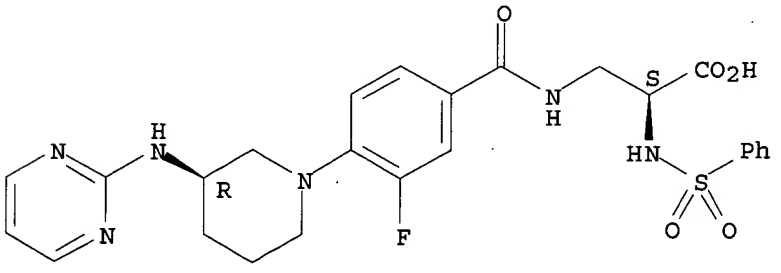
RN 334618-29-0 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334618-31-4 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

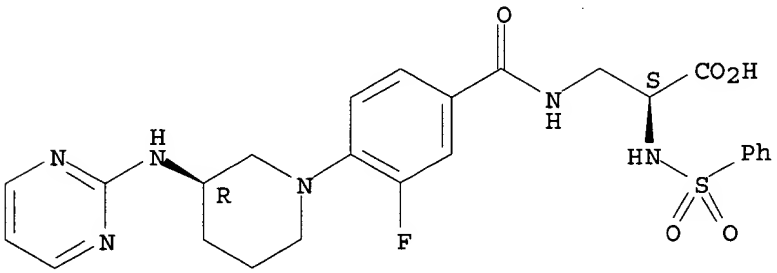


RN 334618-32-5 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

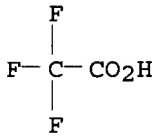
CRN 334618-31-4
CMF C25 H27 F N6 O5 S

Absolute stereochemistry.



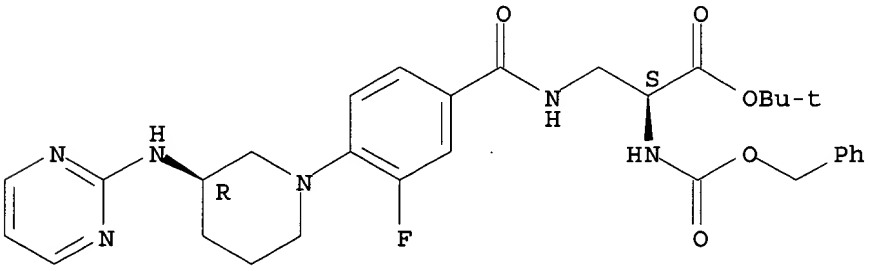
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334618-36-9 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3R)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

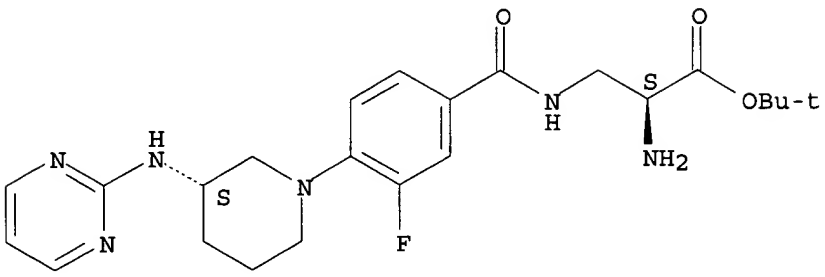
Absolute stereochemistry.



RN 334618-39-2 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

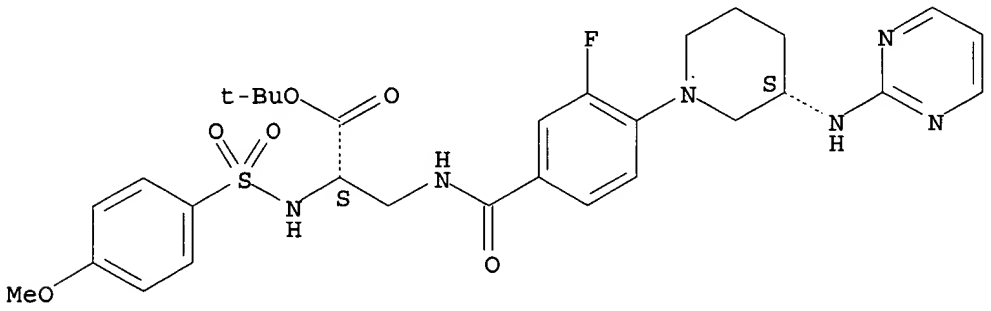
~~09/400,992~~

Absolute stereochemistry. Rotation (+).



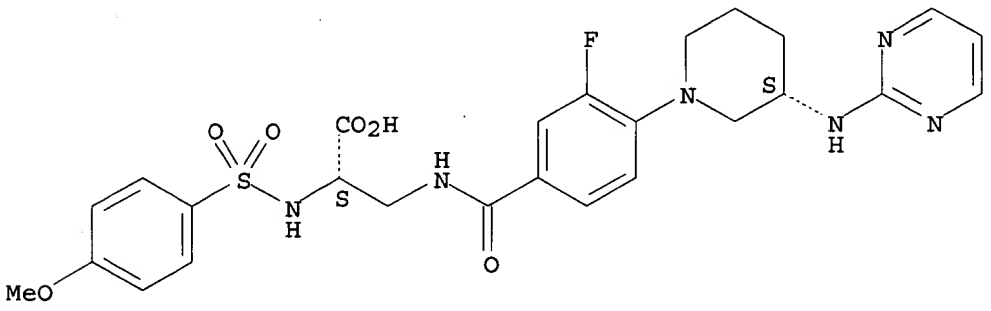
RN 334618-41-6 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-methoxyphenyl)sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334618-43-8 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

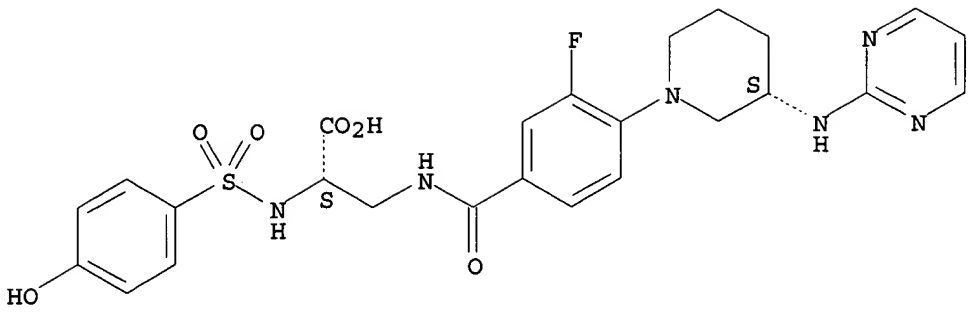
Absolute stereochemistry.



RN 334618-47-2 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-hydroxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

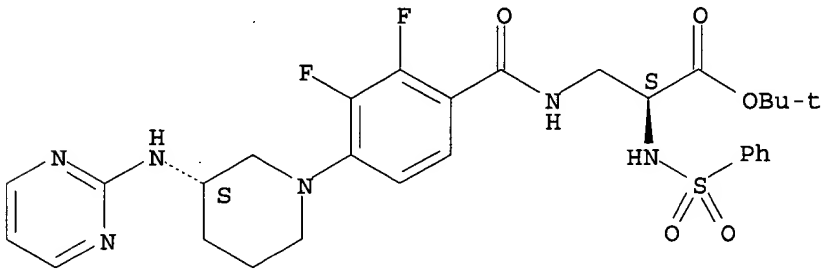
Absolute stereochemistry.

~~09/400,992~~



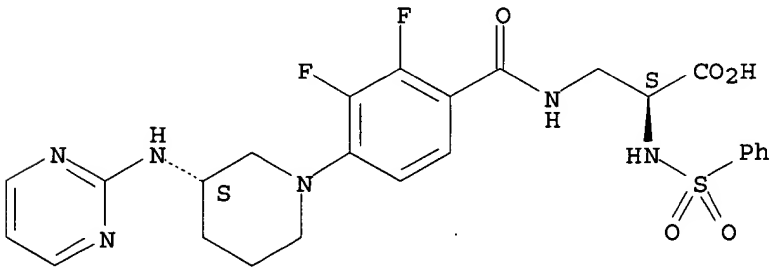
RN 334618-55-2 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334618-57-4 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



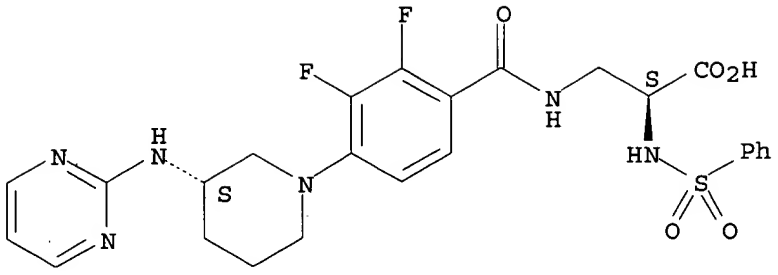
RN 334618-58-5 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 334618-57-4
CMF C25 H26 F2 N6 O5 S

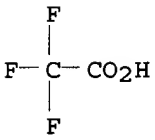
Absolute stereochemistry.

~~09/ 400,992~~



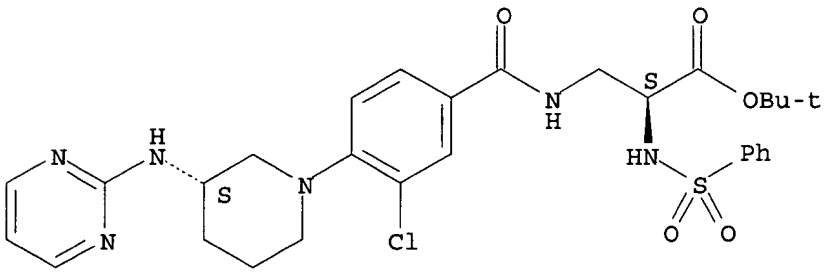
CM 2

CRN 76-05-1
CMF C2 H F3 O2



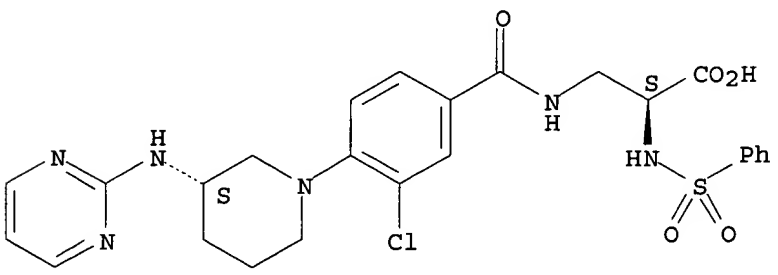
RN 334618-67-6 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334618-69-8 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



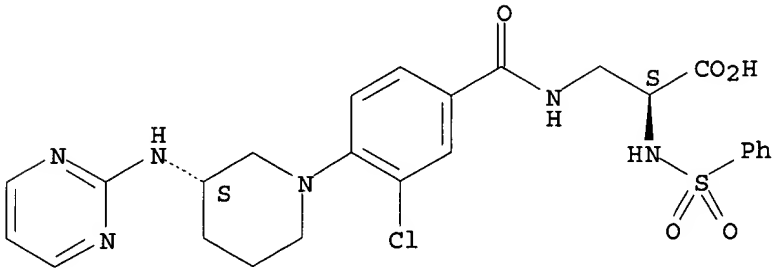
~~09/400,992~~

RN 334618-70-1 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

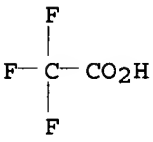
CRN 334618-69-8
CMF C25 H27 Cl N6 O5 S

Absolute stereochemistry. Rotation (+).



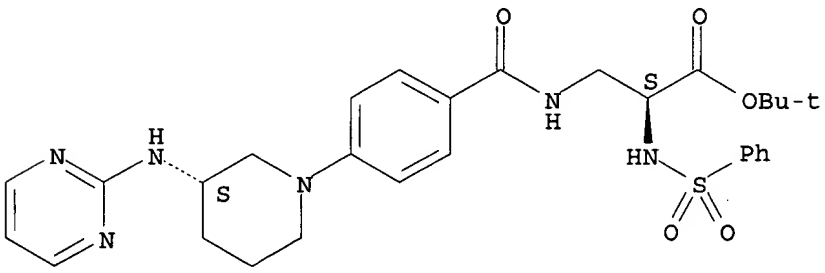
CM 2

CRN 76-05-1
CMF C2 H F3 O2



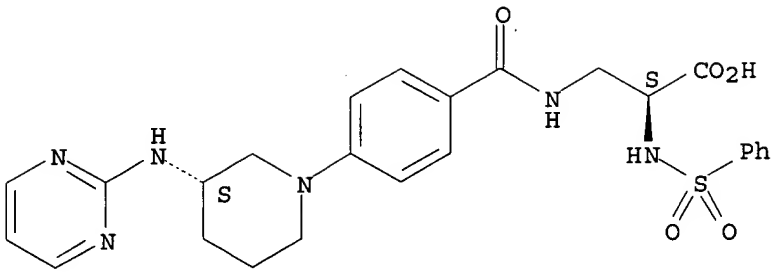
RN 334618-80-3 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334618-82-5 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

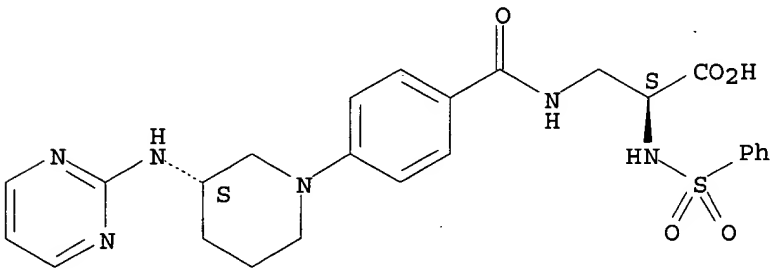


RN 334618-83-6 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

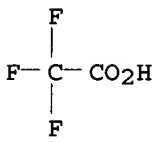
CRN 334618-82-5
CMF C25 H28 N6 O5 S

Absolute stereochemistry.



CM 2

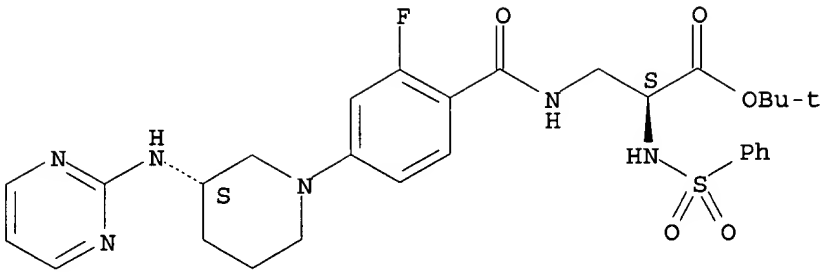
CRN 76-05-1
CMF C2 H F3 O2



RN 334619-04-4 CAPLUS
CN L-Alanine, 3-[[2-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

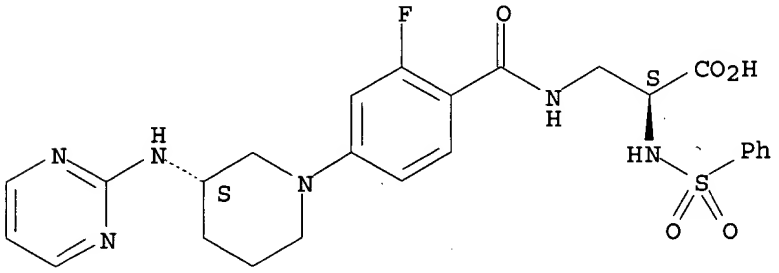
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



RN 334619-06-6 CAPLUS
CN L-Alanine, 3-[[2-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

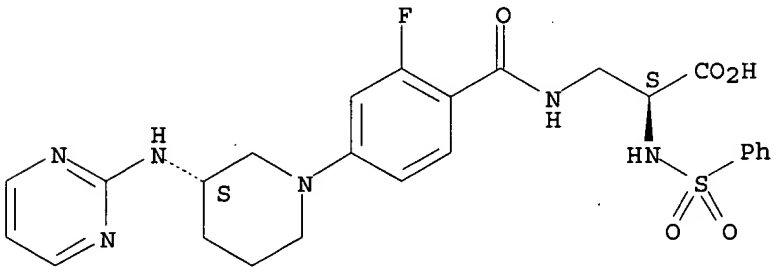


RN 334619-07-7 CAPLUS
CN L-Alanine, 3-[[2-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

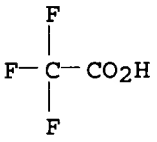
CRN 334619-06-6
CMF C25 H27 F N6 O5 S

Absolute stereochemistry.



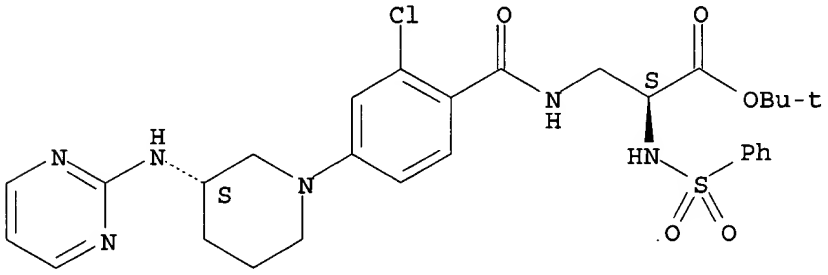
CM 2

CRN 76-05-1
CMF C2 H F3 O2



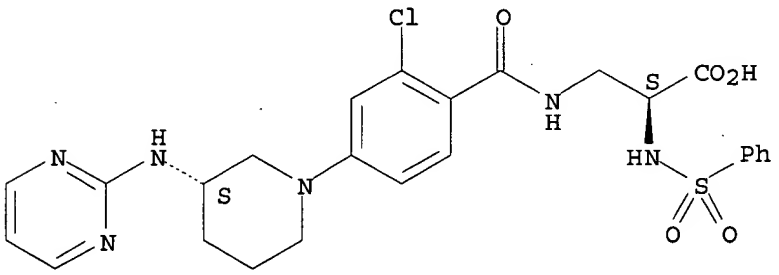
RN 334619-18-0 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334619-20-4 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

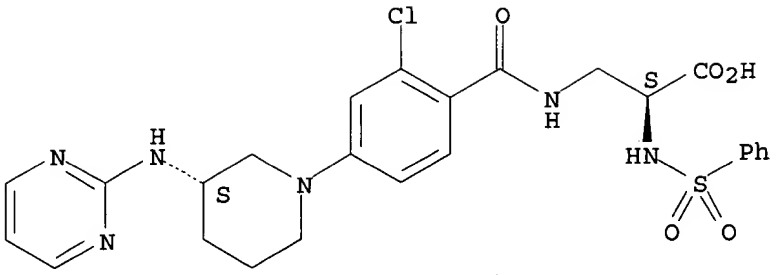


RN 334619-21-5 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

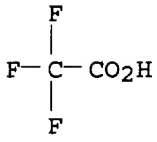
CRN 334619-20-4
CMF C25 H27 Cl N6 O5 S

Absolute stereochemistry.



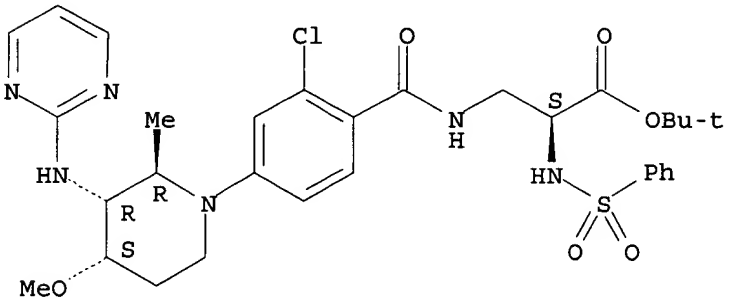
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334619-39-5 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[(2R,3R,4S)-4-methoxy-2-methyl-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

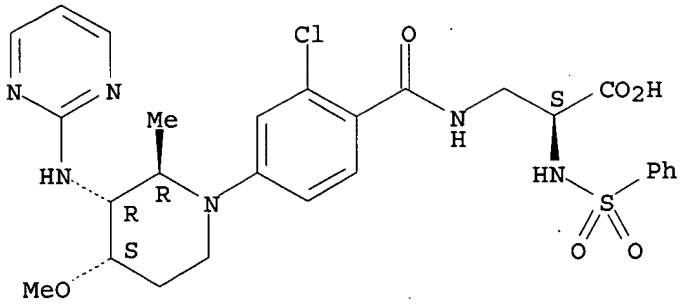
Absolute stereochemistry. Rotation (+).



RN 334619-41-9 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[(2R,3R,4S)-4-methoxy-2-methyl-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~

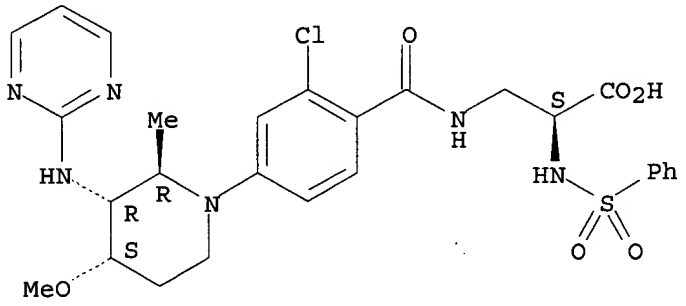


RN 334619-42-0 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[(2R,3R,4S)-4-methoxy-2-methyl-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

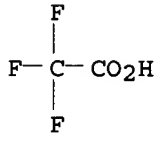
CRN 334619-41-9
CMF C27 H31 Cl N6 O6 S

Absolute stereochemistry.



CM 2

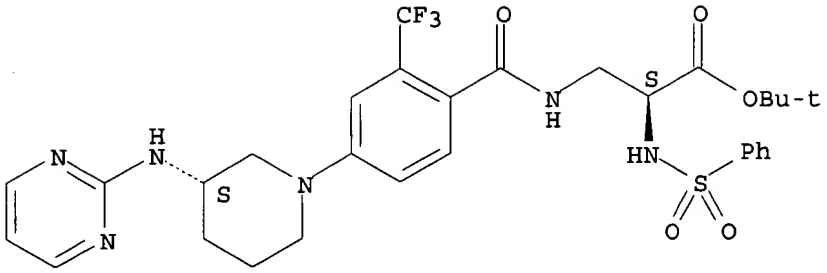
CRN 76-05-1
CMF C2 H F3 O2



RN 334619-53-3 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]-2-(trifluoromethyl)benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

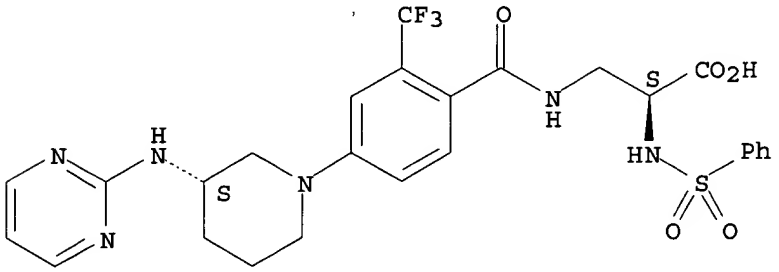
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



RN 334619-55-5 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]-2-(trifluoromethyl)benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

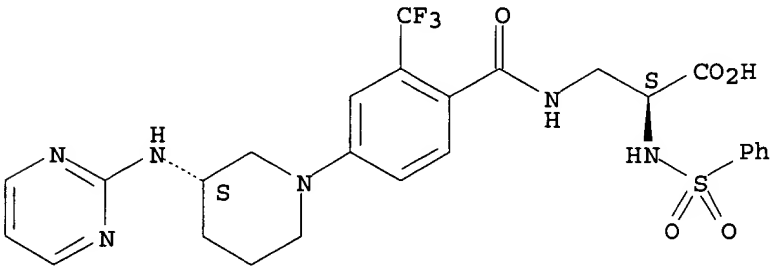


RN 334619-56-6 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]-2-(trifluoromethyl)benzoyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

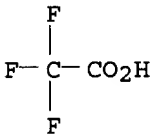
CRN 334619-55-5
CMF C26 H27 F3 N6 O5 S

Absolute stereochemistry.



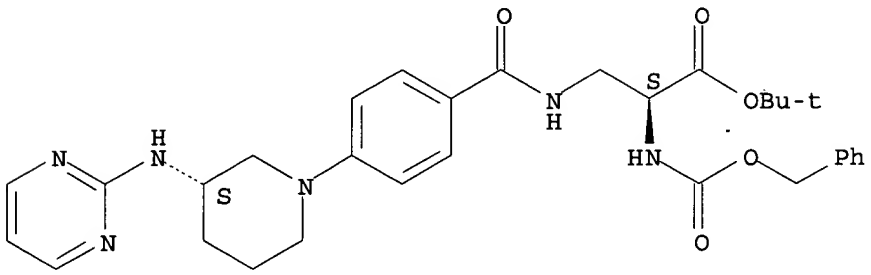
CM 2

CRN 76-05-1
CMF C2 H F3 O2



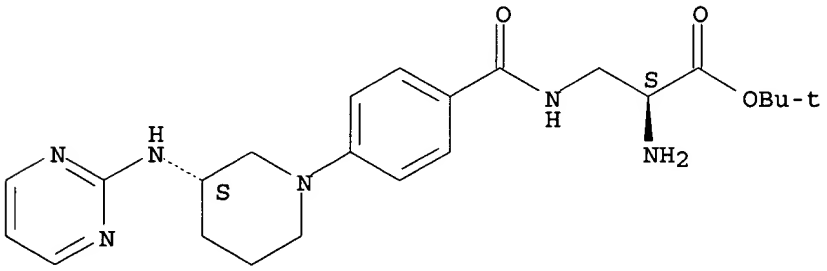
RN 334619-61-3 CAPLUS
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



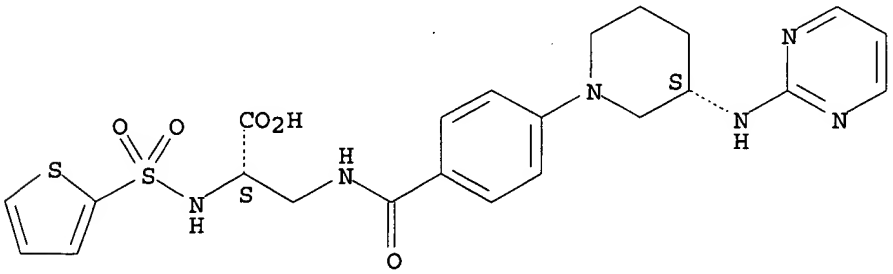
RN 334619-63-5 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334619-67-9 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

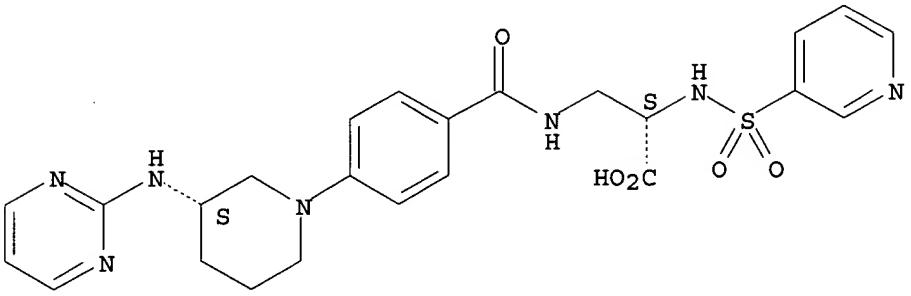
Absolute stereochemistry.



~~09/400,992~~

RN 334619-73-7 CAPLUS
CN L-Alanine, N-(3-pyridinylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

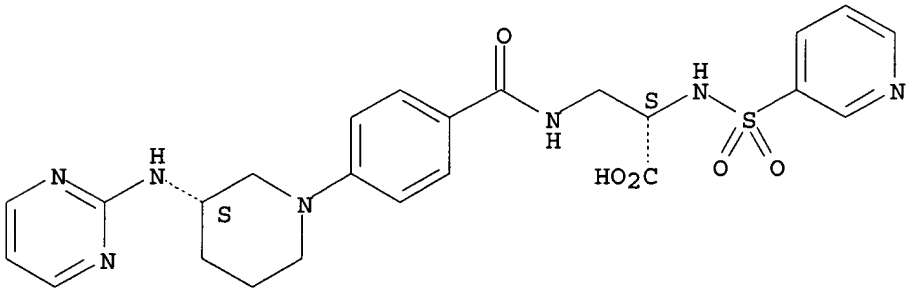


RN 334619-74-8 CAPLUS
CN L-Alanine, N-(3-pyridinylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

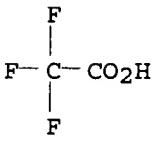
CRN 334619-73-7
CMF C24 H27 N7 O5 S

Absolute stereochemistry.



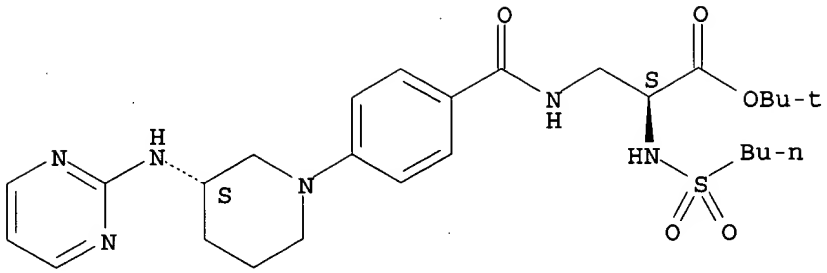
CM 2

CRN 76-05-1
CMF C2 H F3 O2



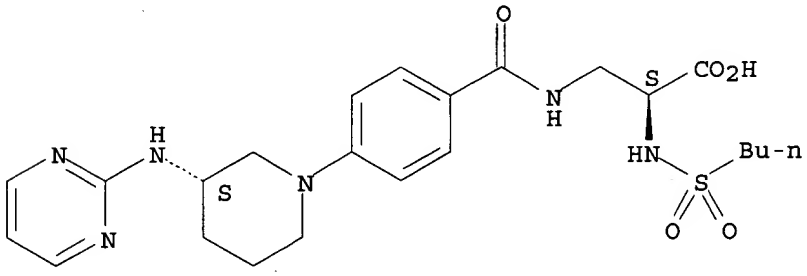
RN 334619-78-2 CAPLUS
CN L-Alanine, N-(butylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334619-80-6 CAPLUS
CN L-Alanine, N-(butylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

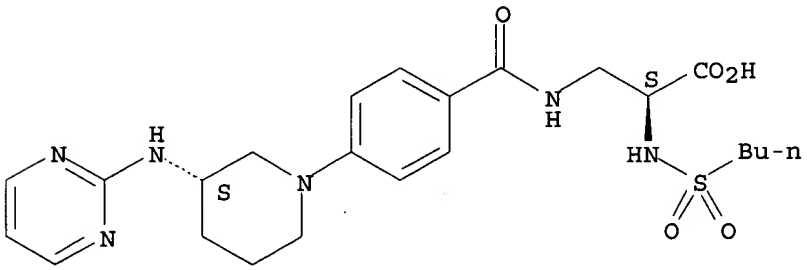


RN 334619-81-7 CAPLUS
CN L-Alanine, N-(butylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 334619-80-6
CMF C23 H32 N6 O5 S

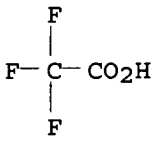
Absolute stereochemistry.



CM 2

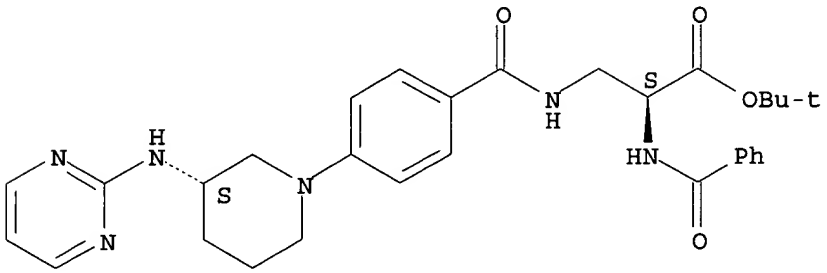
CRN 76-05-1
CMF C2 H F3 O2

~~09/400,992~~



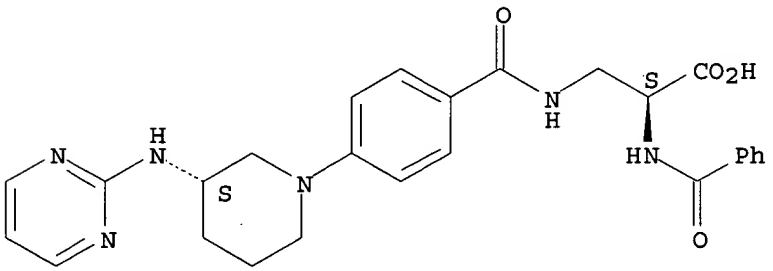
RN 334619-85-1 CAPLUS
CN L-Alanine, N-benzoyl-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 334619-87-3 CAPLUS
CN L-Alanine, N-benzoyl-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



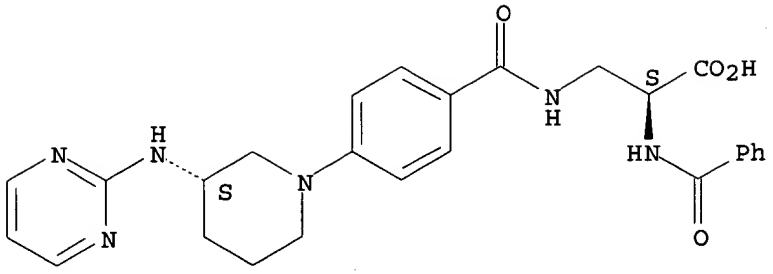
RN 334619-88-4 CAPLUS
CN L-Alanine, N-benzoyl-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 334619-87-3
CMF C26 H28 N6 O4

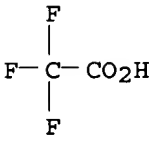
Absolute stereochemistry.

~~09/400,892~~



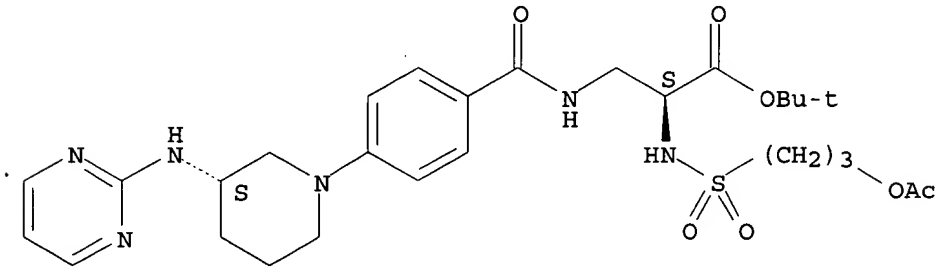
CM 2

CRN 76-05-1
CMF C2 H F3 O2



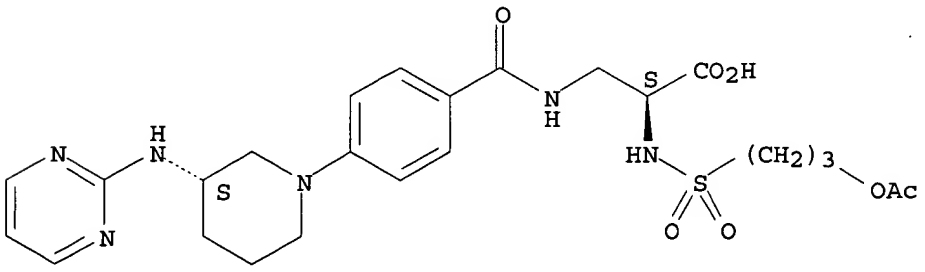
RN 334619-92-0 CAPLUS
CN L-Alanine, N-[[3-(acetyloxy)propyl]sulfonyl]-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334619-94-2 CAPLUS
CN L-Alanine, N-[[3-(acetyloxy)propyl]sulfonyl]-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



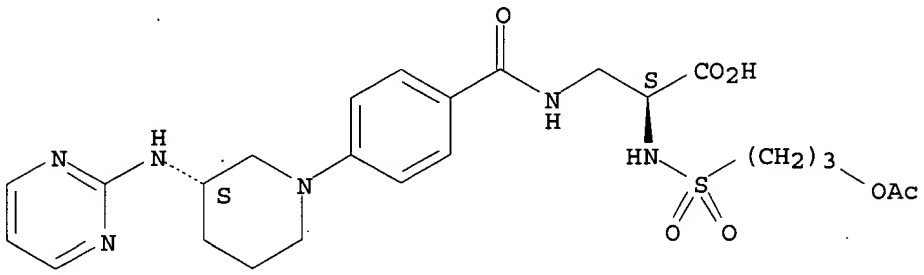
~~09/400,992~~

RN 334619-95-3 CAPLUS
CN L-Alanine, N-[[3-(acetyloxy)propyl]sulfonyl]-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

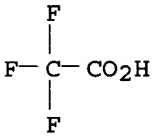
CRN 334619-94-2
CMF C24 H32 N6 O7 S

Absolute stereochemistry.



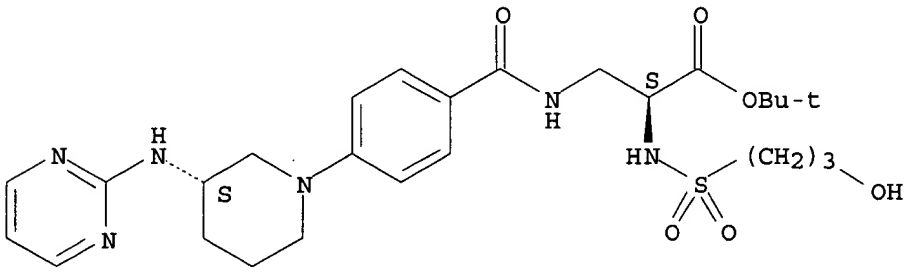
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 334619-99-7 CAPLUS
CN L-Alanine, N-[(3-hydroxypropyl)sulfonyl]-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

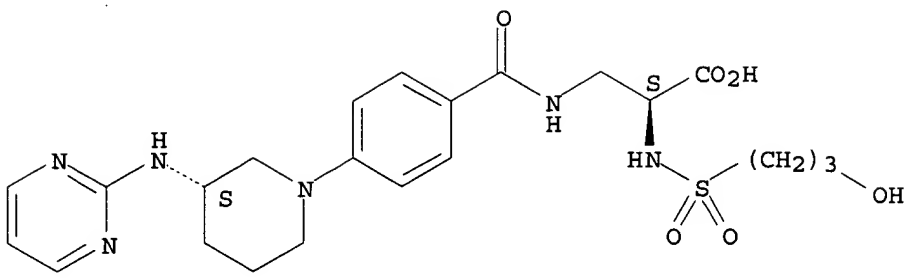
Absolute stereochemistry.



RN 334620-01-8 CAPLUS
CN L-Alanine, N-[(3-hydroxypropyl)sulfonyl]-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

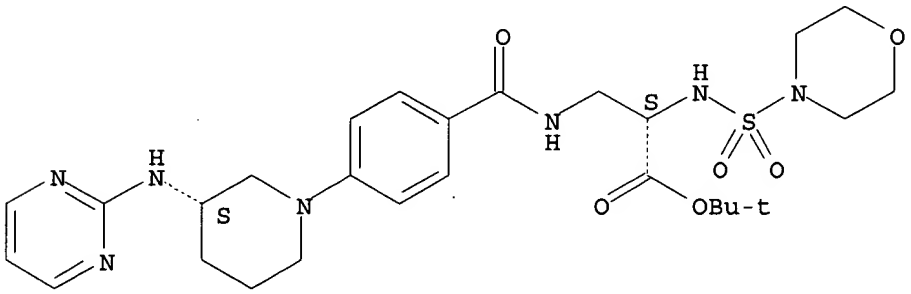
Absolute stereochemistry.

~~09/ 400,952~~



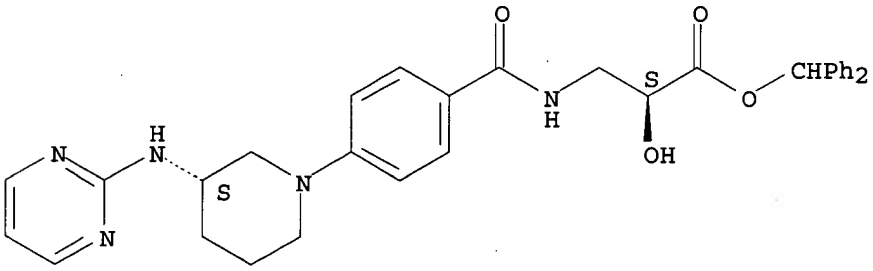
RN 334620-06-3 CAPLUS
CN L-Alanine, N-(4-morpholinylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334620-09-6 CAPLUS
CN Propanoic acid, 2-hydroxy-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, diphenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

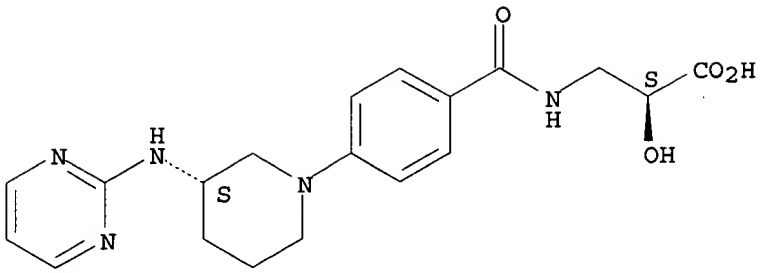
Absolute stereochemistry. Rotation (-).



RN 334620-12-1 CAPLUS
CN Propanoic acid, 2-hydroxy-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

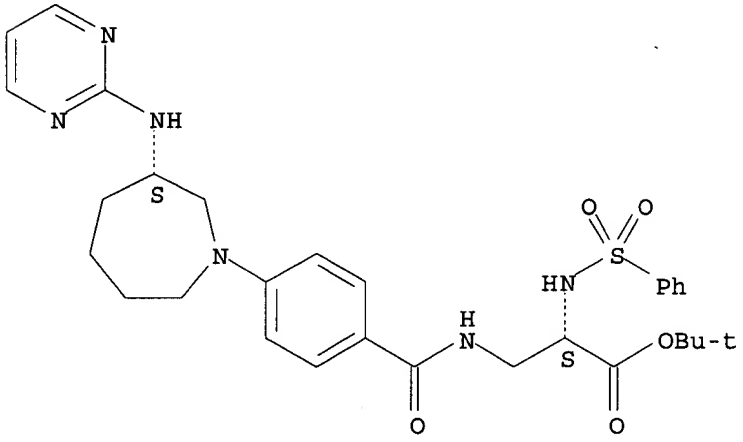
Absolute stereochemistry.

~~09/400,992~~



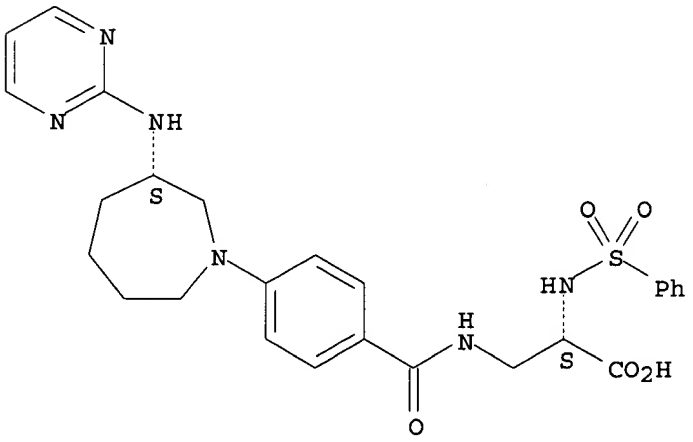
RN 334620-24-5 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-hexahydro-3-(2-pyrimidinylamino)-1H-azepin-1-yl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 334620-27-8 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-hexahydro-3-(2-pyrimidinylamino)-1H-azepin-1-yl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



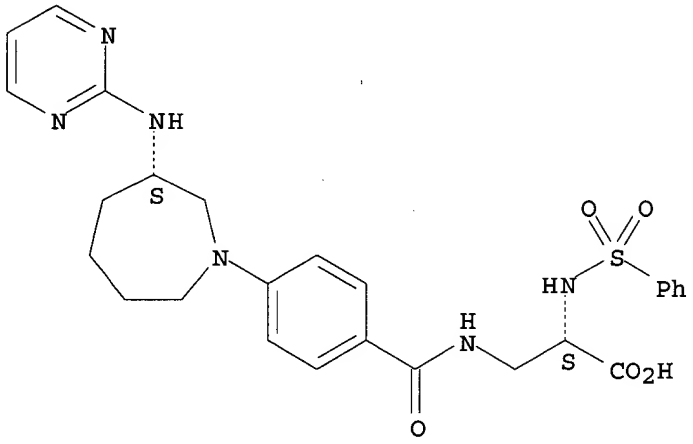
RN 334620-28-9 CAPLUS

CN L-Alanine, 3-[[4-[(3S)-hexahydro-3-(2-pyrimidinylamino)-1H-azepin-1-yl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

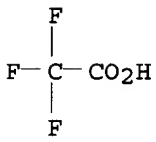
CRN 334620-27-8
CMF C26 H30 N6 O5 S

Absolute stereochemistry.



CM 2

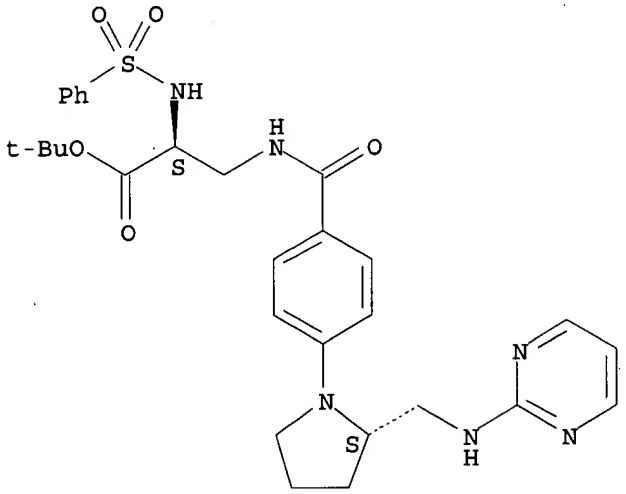
CRN 76-05-1
CMF C2 H F3 O2



RN 334620-65-4 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(2S)-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

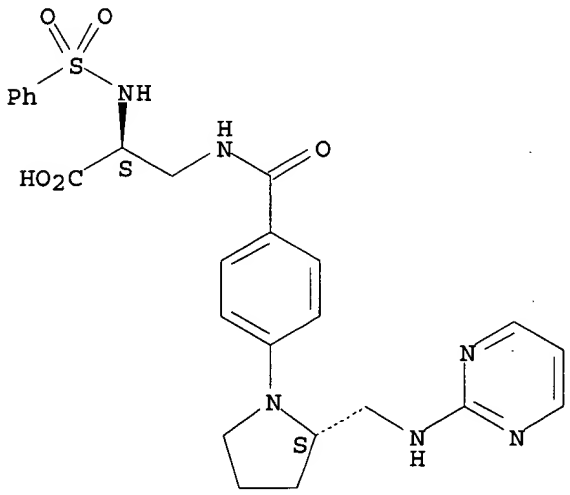
Absolute stereochemistry.

~~09/400,992~~



RN 334620-69-8 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(2S)-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

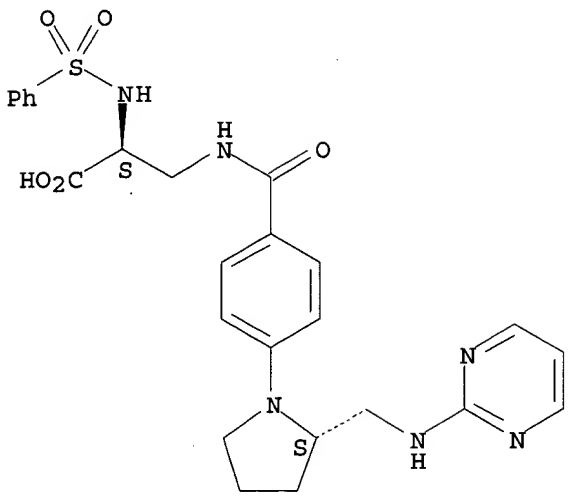


RN 334620-70-1 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(2S)-2-[(2-pyrimidinylamino)methyl]-1-pyrrolidinyl]benzoyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

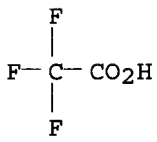
CRN 334620-69-8
CMF C25 H28 N6 O5 S

Absolute stereochemistry.



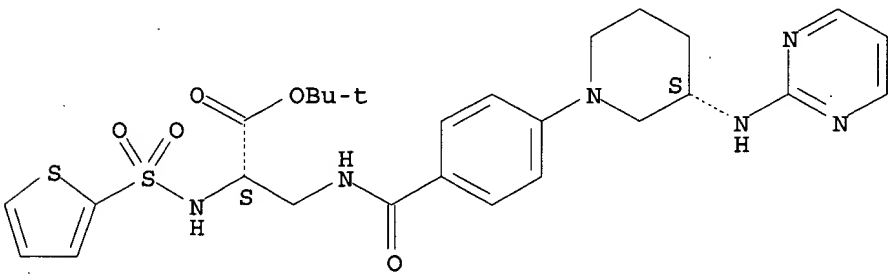
CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **334619-65-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of 3-aminopiperidine derivs. as **integrin** .alpha.v.beta.3 antagonists for preventives or therapeutics)
RN 334619-65-7 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(2-thienylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

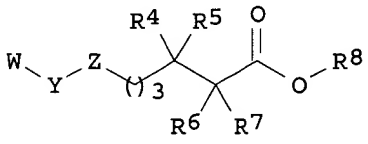
L7 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2003 ACS

~~09/ 400,992~~

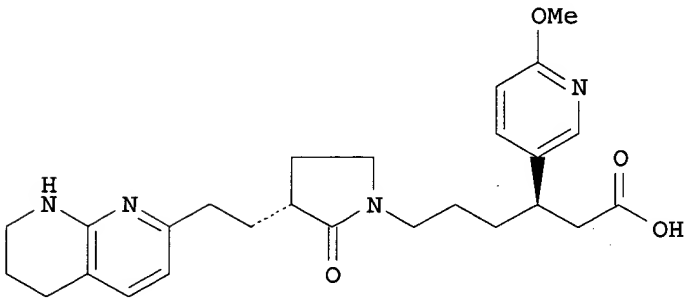
ACCESSION NUMBER: 2001:265252 CAPLUS
DOCUMENT NUMBER: 134:295810
TITLE: Synthesis and use of substituted pyrrolidin-1-yl hexanoic acid derivatives as .alpha..nu..beta.3 and .alpha..nu..beta.5 **integrin** receptors
INVENTOR(S): Askew, Ben C.; Smith, Garry R.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024797	A1	20010412	WO 2000-US27033	20000929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1229910	A1	20020814	EP 2000-967201	20000929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003510360	T2	20030318	JP 2001-527796	20000929
US 6413955	B1	20020702	US 2000-677677	20001002

PRIORITY APPLN. INFO.: US 1999-157490P P 19991004
WO 2000-US27033 W 20000929
OTHER SOURCE(S): MARPAT 134:295810
GI



I



II

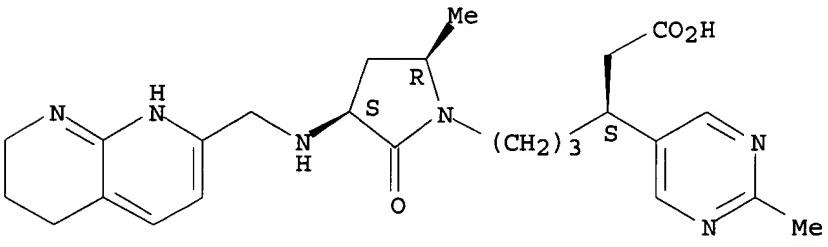
AB Compds. of formula I [wherein; W is a 5 or 6 membered monocyclic (arom.) ring having 1-4 heteroatoms (N, O or S) wherein the ring nitrogen atoms are unsubstituted or substituted with 1 or 2 R1 groups, or a 9-14 membered

polycyclic ring system, wherein the polycyclic ring system has 1-4 heteroatoms (N, O or S) in which the N atoms are substituted as described above; Y is (CH2)m, (CH2)m-(O, NR2 or S(O)0-2)-(CH2)n, etc., where any CH2 can be substituted with 1 or 2 R3 groups, m is 0-3 and n is 0-3; Z is a 5-6 membered heterocyclic system having 1-3 heteroatoms (N, O or S) optionally substituted with one or more R9 group and when 2 R9 substituents are on the same C-atom, they are taken together to form a C3-C6 cycloalkyl group; R1 is H, halo, (cyclo)alkyl, cycloheteroalkyl, aryl(alkyl), amino(alkyl), etc.; R2 is H, alkyl, aryl(alkyl), aminocarbonyl, cycloalkyl, aminoalkyl, etc.; R3 is H, alkyl, aryl(alkyl), halo, OH, oxo, CF3, etc.; R4 and R5 are H, alkyl, aryl(alkyl), halo, OH, alkylcarbonylamino, etc. or taken together the C-atom to form a CO; R6 and R7 are H, alkyl, aryl(alkyl), halo, OH, etc.; R8 is H, alkyl, aryl(alkyl), alkylcarbonyloxyalkyl, etc.; R9 is H, alkyl, aryl, halo, OH, etc.;]. Several examples of I are provided. For instance II was synthesized in 14 steps as a single enantiomer. Compds. I are antagonists of the **integrin** receptors .alpha..nu..beta.3 and/or .alpha..nu..beta.5. Compds. I were found to bind to human .alpha..nu..beta.3 **integrin** with IC50 values less than 10 nM and to the .alpha..nu..beta.5 **integrin** receptor with IC50 values less than 100 nM in competitive binding assays. A bone resorption-pit assay demonstrated the ability of compds. I to inhibit osteoclasts (bovine bone slices). Claimed uses for I are for inhibiting bone resorption, treating and preventing osteoporosis, inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth.

IT **334009-69-7P 334009-70-0P 334009-71-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. and use of substituted pyrrolidin-1-yl hexanoic acid derivs. as .alpha..nu..beta.3 and .alpha..nu..beta.5 **integrin** receptor antagonists)

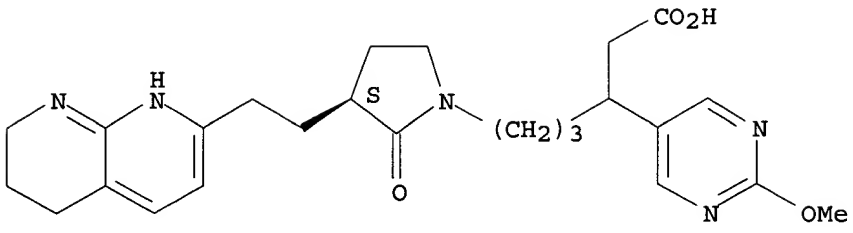
RN 334009-69-7 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[3-[(3S,5R)-5-methyl-2-oxo-3-[[(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)methyl]amino]-1-pyrrolidinyl]propyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



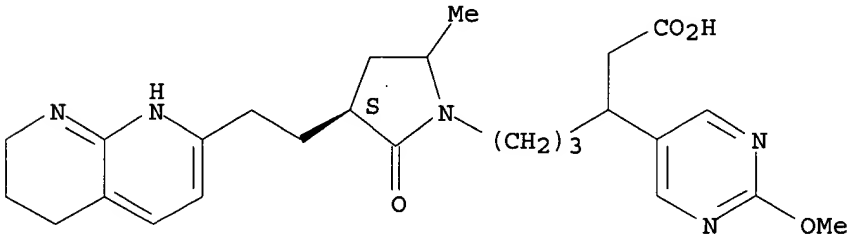
RN 334009-70-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methoxy-.beta.-[3-[(3S)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334009-71-1 CAPLUS
CN 5-Pyrimidinepropanoic acid, 2-methoxy-.beta.-[3-[(3S)-5-methyl-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]propyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:237851 CAPLUS
DOCUMENT NUMBER: 134:252261
TITLE: Preparation of heterocyclylcarbonylamino-modified phenylpropanes and their use as **integrin** VLA-4 binding inhibitors
INVENTOR(S): Yokota, Masaki; Nagashima, Shinya; Sugane, Takashi; Igarashi, Susumu; Moridaira, Koichiro; Miura, Ayanori; Ikeda, Masaru; Takeuchi, Makoto
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001089448	A2	20010403	JP 1999-271096	19990924

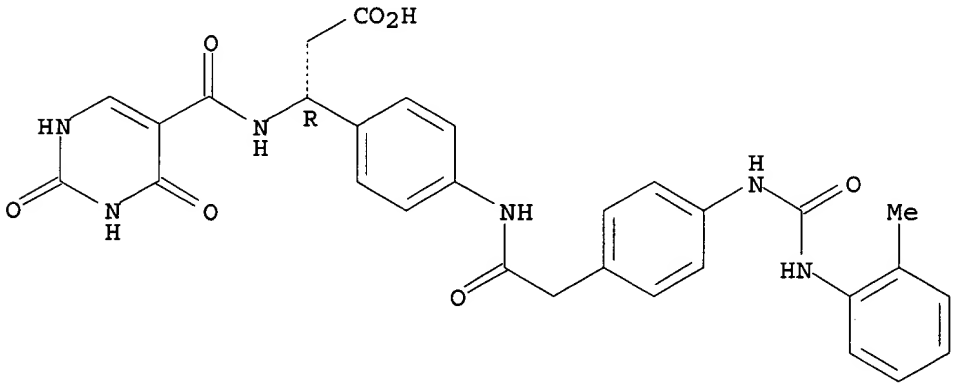
PRIORITY APPLN. INFO.: JP 1999-271096 19990924
OTHER SOURCE(S): MARPAT 134:252261
AB 4-RcCH2CONRdC6H4CH(NReCORb)CH2CO2Ra [Ra = H, ester residue (prodrug); Rb = morpholino, 2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl; Rc = (un)substituted (hetero)aryl; Rd, Re = H, lower alky], useful for treatment of asthma, allergy, rheumatoid arthritis, autoimmune disease, rejection, inflammation, arteriosclerosis, cancer metastasis, diabetes, etc., are prepd. Thus, a soln. of 5-methoxyindoleacetic acid and Et (RS)-3-(4-aminophenyl)-3-[(morpholine-4-carbonyl)amino]propanoate in DMF was treated with WSC.HCl and HOBt at room temp. for 20 h to give the corresponding amide.

~~09/400,992~~

IT **331681-16-4P 331681-45-9P 331681-46-0P**
331681-47-1P 331681-48-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of heterocyclylcarbonylamino-modified phenylpropanes as **integrin** VLA-4 binding inhibitors for treatment of diseases)

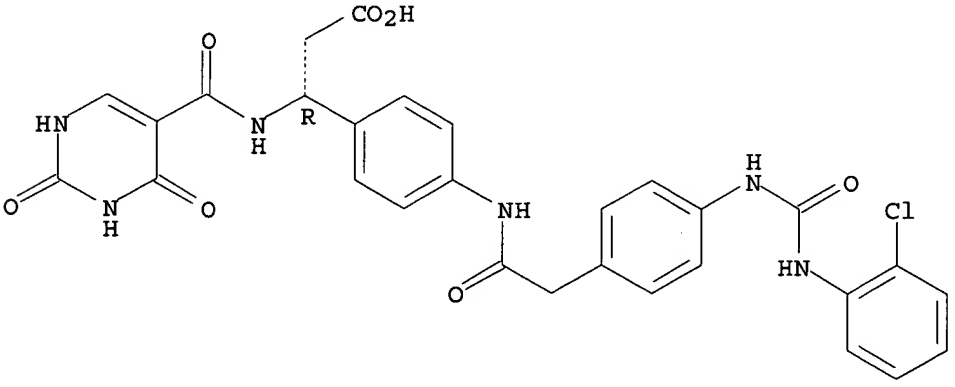
RN 331681-16-4 CAPLUS
CN Benzenepropanoic acid, 4-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-.beta.-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

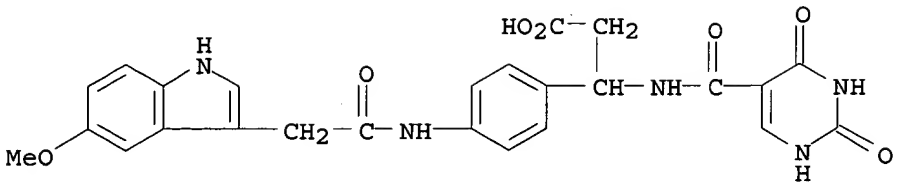


RN 331681-45-9 CAPLUS
CN Benzenepropanoic acid, 4-[[[4-[[[(2-chlorophenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-.beta.-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

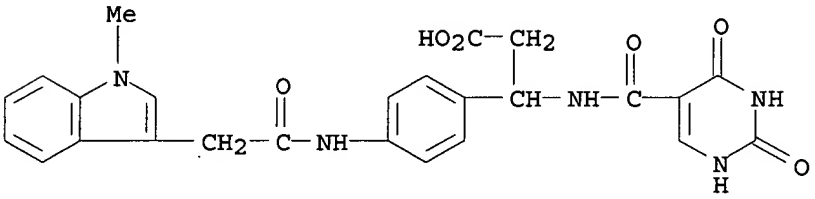
Absolute stereochemistry.



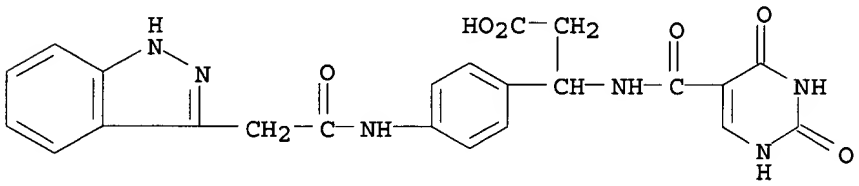
RN 331681-46-0 CAPLUS
CN Benzenepropanoic acid, 4-[[(5-methoxy-1H-indol-3-yl)acetyl]amino]-.beta.-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 331681-47-1 CAPLUS
CN Benzenepropanoic acid, 4-[[(1-methyl-1H-indol-3-yl)acetyl]amino]-.beta.-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 331681-48-2 CAPLUS
CN Benzenepropanoic acid, 4-[(1H-indazol-3-ylacetyl)amino]-.beta.-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



L7 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:152648 CAPLUS
DOCUMENT NUMBER: 134:193442
TITLE: Preparation of pyridinyl- and pyrimidinylaminoalkoxyphenylbutyric acid derivatives and analogs as .alpha.v.beta.3 **integrin** inhibitors
INVENTOR(S): Jonczyk, Alfred; Schadt, Oliver; Goodman, Simon
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014337	A1	20010301	WO 2000-EP7590	20000804

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

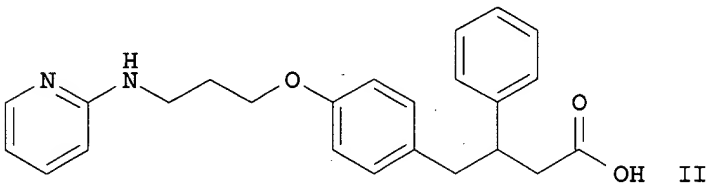
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19939980	A1	20010301	DE 1999-19939980	19990824
BR 2000013502	A	20020507	BR 2000-13502	20000804
EP 1206455	A1	20020522	EP 2000-958381	20000804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003507457	T2	20030225	JP 2001-518426	20000804
NO 2002000885	A	20020222	NO 2002-885	20020222

PRIORITY APPLN. INFO.: DE 1999-19939980 A 19990824
WO 2000-EP7590 W 20000804

OTHER SOURCE(S): MARPAT 134:193442

GI



II

AB The invention relates to novel compds. of formula X-Y-Z-R1-CH2-R2(R4)-CH2-CO-R5, [I; wherein: X = amidino, guanidino, alkyliminoylamino, heterocyclyl or heterocyclylamino with optional amino substituent(s); Y = (CH2)n, (CH2)m-C6H3(R3)-(CH2)o or N/O/S hetero-chain analogs; Z = O, NH, NA, CH(OH), CH(OA), CHA, CA2, S; A = alkyl; R1 = (un)substituted Ph; R2 = N, CH, CA; R3 = H, F, Cl, Br, A, OA, OCF3; R4 = (un)substituted Ph, naphthyl, heterocyclyl; R5 = OH, OA, NH2, NHA, NA2; n = 1-12; m, o = 0-12], and their physiol. acceptable salts and solvates. I are biol. active as .alpha.v.beta.3 **integrin** ligands, particularly as antagonists. Claimed uses include treatment of thromboses, heart infarct, coronary artery disease, arteriosclerosis, tumors, osteoporosis, fibrosis, inflammation, infection, or psoriasis, as well as promotion of wound healing. Several examples were prepd. and/or claimed. For instance, 4-benzyloxybenzyl chloride underwent Grignard reaction with 2-cyano-3-phenylacrylic acid Et ester, followed by acid hydrolysis and decarboxylation, to give 4-(4-hydroxyphenyl)-3-phenylbutyric acid. The latter acid underwent esterification, Mitsunobu reaction with 3-(1-oxypyridin-2-ylamino)propan-1-ol, deoxygenation with PCl3, and sapon., to give title compd. II. In a test for inhibition of binding of vitronectin to isolated .alpha.v.beta.3 receptors, II had an IC50 of 5.3 nM.

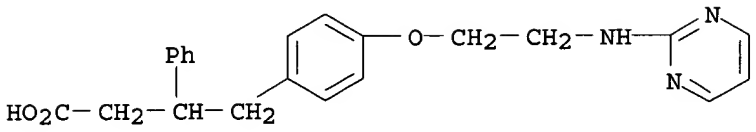
IT **328092-14-4P**, 3-Phenyl-4-[4-[2-(pyrimidin-2-ylamino)ethoxy]phenyl]butyric acid trifluoroacetate **328092-19-9P**, 3-Phenyl-4-[4-[3-(pyrimidin-2-ylamino)propoxy]phenyl]butyric acid trifluoroacetate **328092-25-7P**, 3-Phenyl-4-[4-[4-(pyrimidin-2-ylamino)butoxy]phenyl]butyric acid trifluoroacetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(drug candidate; prepn. of pyridinyl- and pyrimidinylaminoalkoxyphenylbutyric acid derivs. and analogs as .alpha.v.beta.3 **integrin** inhibitors)

RN 328092-14-4 CAPLUS

CN Benzenebutanoic acid, .beta.-phenyl-4-[2-(2-pyrimidinylamino)ethoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

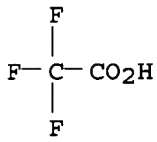
CM 1

CRN 328092-13-3
CMF C22 H23 N3 O3



CM 2

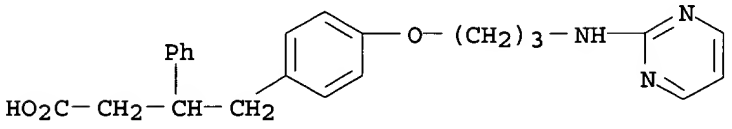
CRN 76-05-1
CMF C2 H F3 O2



RN 328092-19-9 CAPLUS
CN Benzenebutanoic acid, .beta.-phenyl-4-[3-(2-pyrimidinylamino)propoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

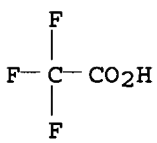
CM 1

CRN 328092-18-8
CMF C23 H25 N3 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

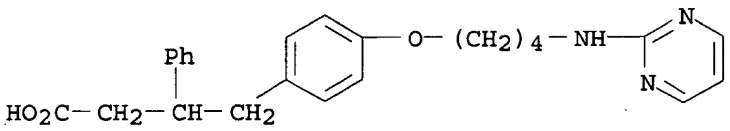


RN 328092-25-7 CAPLUS
CN Benzenebutanoic acid, .beta.-phenyl-4-[4-(2-pyrimidinylamino)butoxy]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

09/400,992

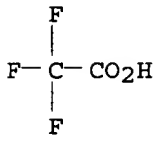
CM 1

CRN 328092-24-6
CMF C24 H27 N3 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:115127 CAPLUS
DOCUMENT NUMBER: 134:163066
TITLE: Preparation and effect of .omega.-amino-.alpha.-hydroxycarboxylic acid derivatives having **integrin** .alpha.v.beta.3 antagonism
INVENTOR(S): Ajito, Keiichi; Yahata, Naokazu; Ishikawa, Minoru; Kubota, Dai; Murakami, Shoichi; Yamamoto, Mikio; Fujishima, Kazuyuki; Gomi, Shuichi; Ouchi, Shokichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010844	A1	20010215	WO 2000-JP5177	20000802
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1209152	A1	20020529	EP 2000-949959	20000802
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

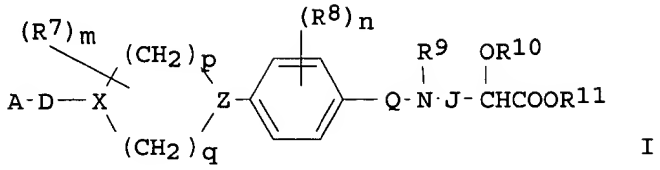
PRIORITY APPLN. INFO.: JP 1999-222098 A 19990805

~~09/400,992~~

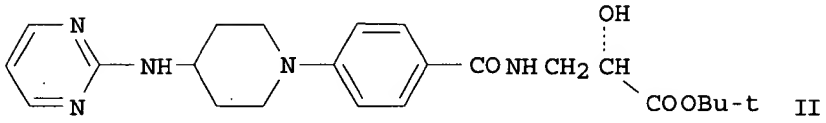
WO 2000-JP5177 W 20000802

OTHER SOURCE(S): MARPAT 134:163066

GI



I



II

AB Title compds. [I; wherein A represents an optionally substituted 5- to 7-membered heterocyclic group contg. 2 nitrogen atoms which may be condensed with other ring(s) or C(NR2)(:NR3); D represents a bond, NR4,O or S; X and Z represent each CH or N; R7 and R8 represent each C1-6 alkyl, halogeno, oxygen, etc.; Q represents CO, CHR13 or CHOR13; J represents a bond or C1-3 alkylene; R1 to R4, R9 to R11 and R13 represent each hydrogen, alkyl, etc.; m is an integer of from 0 to 5; n is an integer of from 0 to 4; and p and q are each an integer of from 1 to 3], which are highly sol. in water and having an **integrin** .alpha.v.beta.3 antagonism, and pharmaceutical acceptable salts are prepd. Thus, the title compd. II was prepd. and tested.

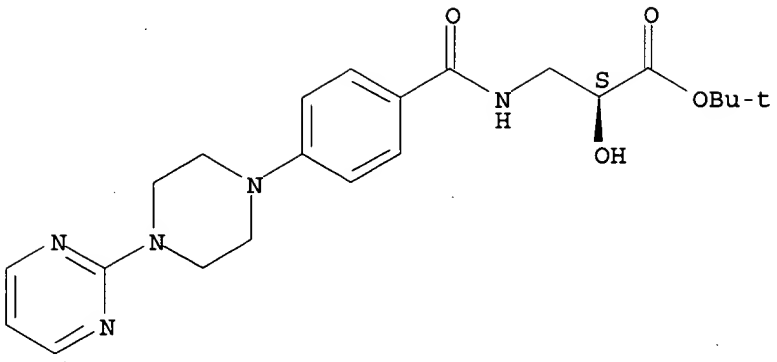
IT **324781-18-2P 324781-22-8P 324781-24-0P**
324781-25-1P 324781-26-2P 324781-29-5P
324781-30-8P 324781-32-0P 324781-33-1P
324781-34-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. and effect of .omega.-amino-.alpha.-hydroxycarboxylic acid derivs. having **integrin** .alpha.v.beta.3 antagonism)

RN 324781-18-2 CAPLUS

CN Propanoic acid, 2-hydroxy-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

~~09/400,992~~

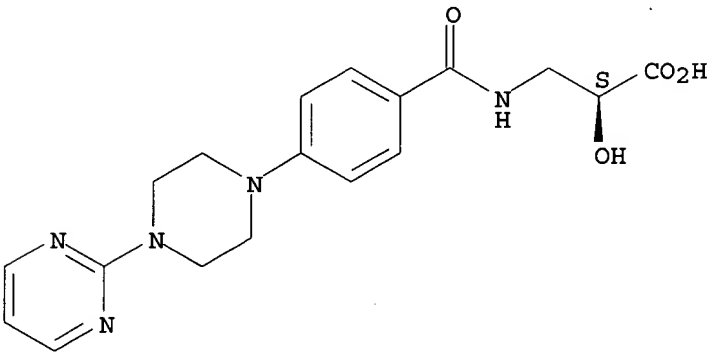


RN 324781-22-8 CAPLUS
CN Propanoic acid, 2-hydroxy-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, (2S)-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

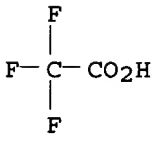
CRN 324781-21-7
CMF C18 H21 N5 O4

Absolute stereochemistry. Rotation (-).



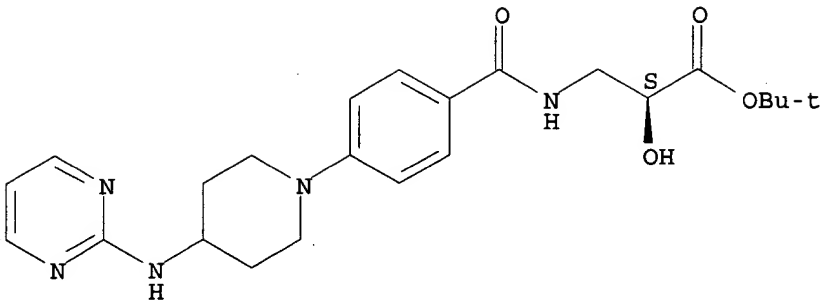
CM 2

CRN 76-05-1
CMF C2 H F3 O2



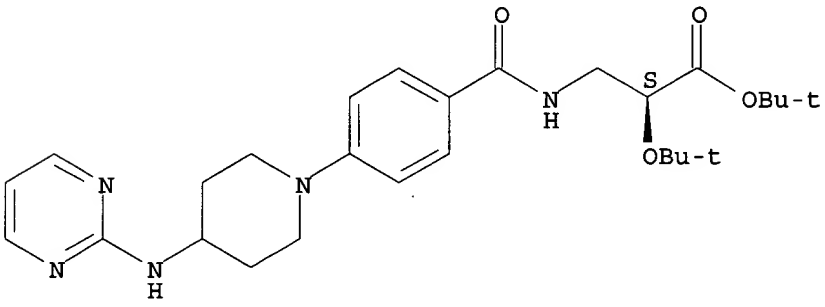
RN 324781-24-0 CAPLUS
CN Propanoic acid, 2-hydroxy-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



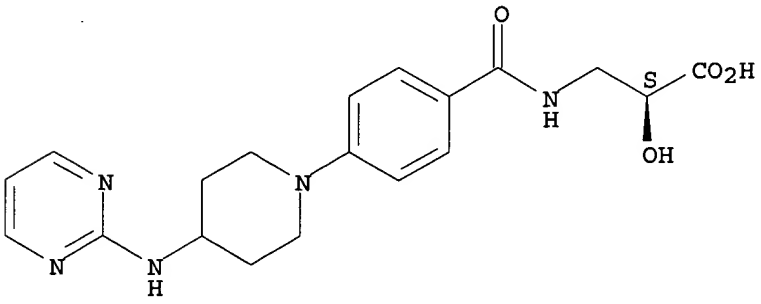
RN 324781-25-1 CAPLUS
CN Propanoic acid, 2-(1,1-dimethylethoxy)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



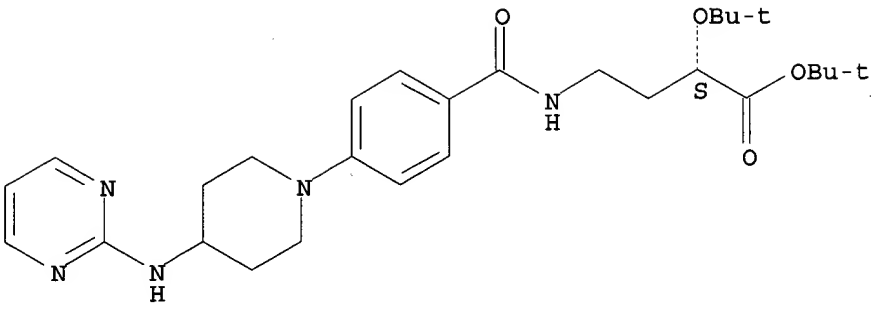
RN 324781-26-2 CAPLUS
CN Propanoic acid, 2-hydroxy-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



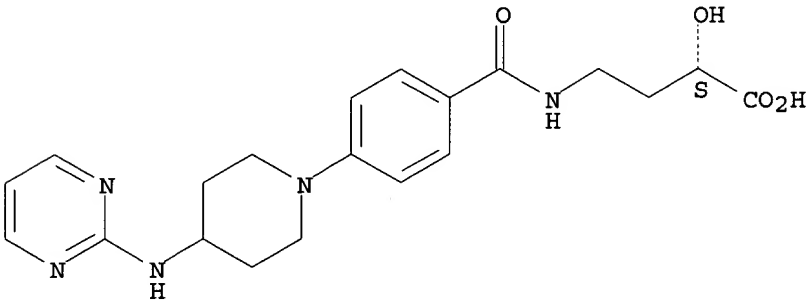
RN 324781-29-5 CAPLUS
CN Butanoic acid, 2-(1,1-dimethylethoxy)-4-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



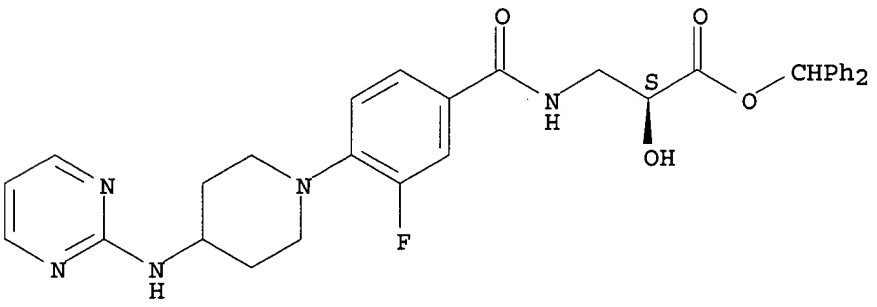
RN 324781-30-8 CAPLUS
CN Butanoic acid, 2-hydroxy-4-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 324781-32-0 CAPLUS
CN Propanoic acid, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-2-hydroxy-, diphenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

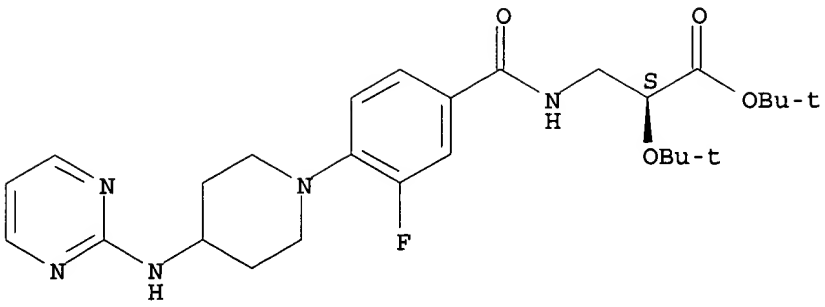
Absolute stereochemistry. Rotation (-).



RN 324781-33-1 CAPLUS
CN Propanoic acid, 2-(1,1-dimethylethoxy)-3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

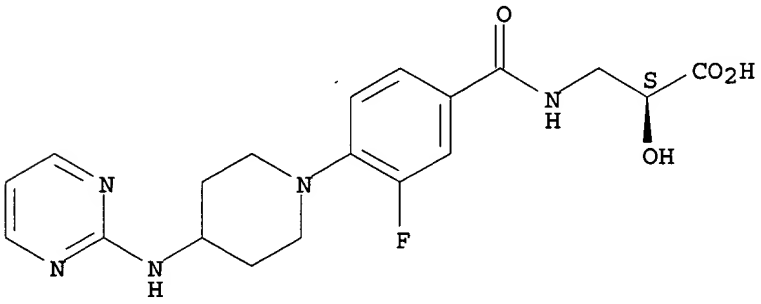
Absolute stereochemistry. Rotation (-).

09/400,992



RN 324781-34-2 CAPLUS
CN Propanoic acid, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-2-hydroxy-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



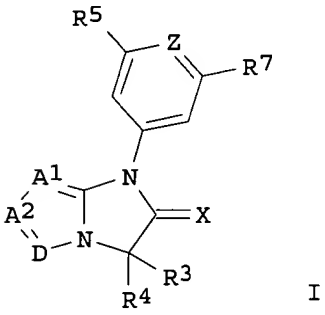
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:78387 CAPLUS
DOCUMENT NUMBER: 134:131538
TITLE: Preparation of imidazoimidazoles and triazoles as anti-inflammatory agents
INVENTOR(S): Wu, Jiang-Ping; Kelly, Terence Alfred; Lemieux, Rene M.; Goldberg, Daniel R.; Emeigh, Jonathan Emilian; Sorcek, Ronald J.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 368 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007440	A1	20010201	WO 2000-US18884	20000712

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6492408 B1 20021210 US 2000-604312 20000627
BR 2000012666 A 20020409 BR 2000-12666 20000712
EP 1216247 A1 20020626 EP 2000-948618 20000712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
JP 2003505460 T2 20030212 JP 2001-512524 20000712
NO 2002000275 A 20020204 NO 2002-275 20020118
PRIORITY APPLN. INFO.: US 1999-144905P P 19990721
US 1999-150939P P 19990826
WO 2000-US18884 W 20000712
OTHER SOURCE(S): MARPAT 134:131538
GI



I

AB Compds. I {A1 = N, CH; A2 = N, CH, CR'; R' = halo, cyano, alkoxy, alkoxycarbonyl, alkylsulfonyl; D = N, CH, CR1, C(SO2R1), C[S(:O)R1], C(CHO), C(SR1a), C(OR1a), C(NHR1a); R1, R1a = (substituted) alkyl, cycloalkyl, aryl, or heteroaryl groups, alkyl groups contg. 2-6 carbons substituted with carboxylate, phosphonate, sulfonate, amidine, or guanidine moieties, amino, halogen, cyano; R3 = H, alkyl, cycloalkyl, alkoxy or amino substituted alkyl, cycloalkyl; R4 = substituted arylmethyl; R5 = Cl, F3C; R7 = H, halo, Me, cyano, O2N, F3C; X = O, S; if Z = N or CH, R7 = Cl, F3C, cyano, O2N; Z = N, CR6 where R6 = H, halo, Me, cyano, F3C}, based mostly on imidazo[1,2-a]imidazole and imidazo[1,2-a]triazole nuclei, are prepd. as inhibitors of the binding of leukointegrins to cell adhesion mols. in the treatment or prevention of inflammatory and immune cell-mediated diseases. E.g., (R)-I (A1 = N; A2 = D = CH; R3 = Me; R4 = 4-BrC6H4CH2; R5 = R7 = Cl; X = O; Z = CH) (II) was prepd. from (R)-.alpha.-methyl-4-bromophenylalanine Me ester and 3,5-dichlorophenylisothiocyanate by heating in 1,4-dioxane to give a thiohydrantoin which was treated with N-(triphenylphosphoranylidene)-1,3-dioxolan-2-ylmethylamine [prepd. from 2-(azidomethyl)-1,3-dioxolane and triphenylphosphine] to give a dioxolanylmethyliminoimidazolidinone deriv.; treatment of the intermediate with trifluoroacetic acid and heating at 90.degree. overnight gave II with m.p. 36-37.5.degree.. I inhibited binding of leukointegrins to cell adhesion mols. with Kd<10 .mu.M.

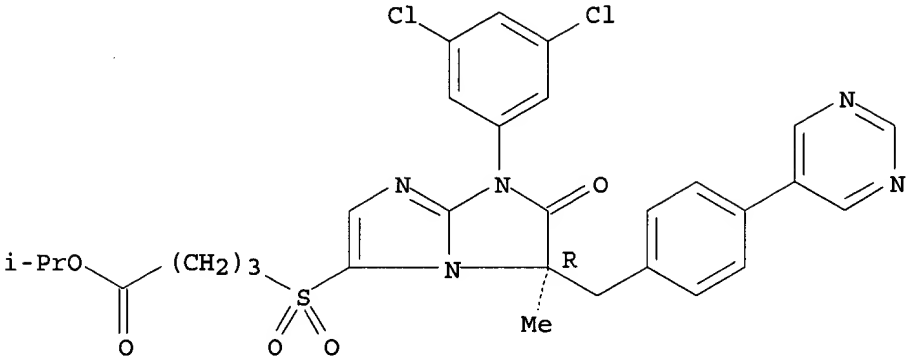
IT **321723-21-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of imidazoimidazole and imidazotriazole derivs. as inhibitors of leukointegrin binding to cell adhesion mols. in the treatment of inflammatory and immune-cell mediated diseases)

RN 321723-21-1 CAPLUS

CN Butanoic acid, 4-[[(3R)-1-(3,5-dichlorophenyl)-2,3-dihydro-3-methyl-2-oxo-3-[[4-(5-pyrimidinyl)phenyl]methyl]-1H-imidazo[1,2-a]imidazol-5-

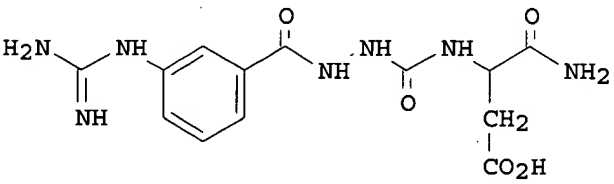
yl]sulfonyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:53692 CAPLUS
DOCUMENT NUMBER: 134:223033
TITLE: Nonpeptidic .alpha.v.beta.3 **integrin** antagonist libraries: on-bead screening and mass spectrometric identification without tagging
AUTHOR(S): Gibson, Christoph; Sulyok, Gabor A. G.; Hahn, Diane; Goodman, Simon L.; Holzemann, Gunter; Kessler, Horst
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Tech. Univ. Munchen, Garching, 85747, Germany
SOURCE: Angewandte Chemie, International Edition (2001), 40(1), 165-169
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

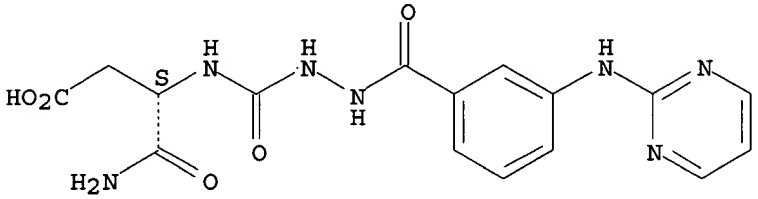
AB The authors report on their work for identifying low mol. wt. **integrin** ligands through application of combinatorial solid-phase synthesis, biol. on-bead evaluation, and mass spectrometric identification of selected compds., which eliminates the reduced efficiency of tagged-bead methods of synthesis. A combinatorial library of aza-RGD mimetic compds., e.g. (I), were synthesized using a split bead method, and tested for activity using a sol. .alpha.v.beta.3 **integrin** receptor system. Beads contg. active compds. were cleaved, and the active compds. identified by mass-spectra, which were unique for individual compds. due to limitations of the component selection method.

IT **329729-77-3P 329729-78-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation)
(prepn. and screening of aza-RGD mimetics using combinatorial synthesis, .alpha.v.beta.3 **integrin** recognition, and mass-spectral anal. techniques)

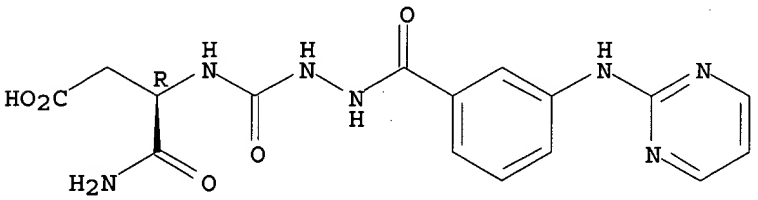
RN 329729-77-3 CAPLUS
CN Benzoic acid, 3-(2-pyrimidinylamino)-, 2-[[[(1S)-2-amino-1-(carboxymethyl)-2-oxoethyl]amino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 329729-78-4 CAPLUS
CN Benzoic acid, 3-(2-pyrimidinylamino)-, 2-[[[(1R)-2-amino-1-(carboxymethyl)-2-oxoethyl]amino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861451 CAPLUS
DOCUMENT NUMBER: 134:29136
TITLE: Novel nonanoic acid derivatives as alpha V **integrin** receptor antagonists
INVENTOR(S): Coleman, Paul J.; Duggan, Mark E.; Halczenko, Wasyl; Hartman, George D.; Hutchinson, John H.; Meissner, Robert S.; Patane, Michael A.; Perkins, James J.; Wang, Jiabing; Breslin, Michael J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072801	A2	20001207	WO 2000-US14901	20000530

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,

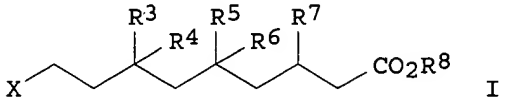
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000011108	A	20020319	BR 2000-11108	20000530
EP 1187592	A2	20020320	EP 2000-942652	20000530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 749351	B2	20020627	AU 2000-57246	20000530
US 6410526	B1	20020625	US 2000-583522	20000531
NO 2001005858	A	20020204	NO 2001-5858	20011130

PRIORITY APPLN. INFO.: US 1999-137101P P 19990602
US 2000-179216P P 20000131
WO 2000-US14901 W 20000530

OTHER SOURCE(S): MARPAT 134:29136

GI



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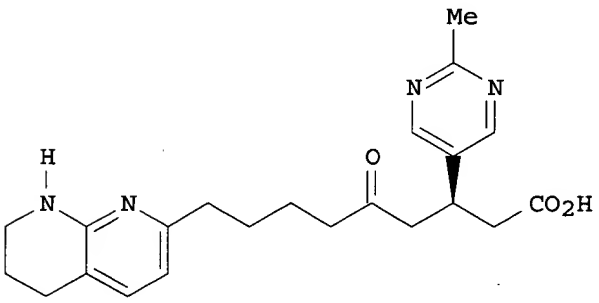


II

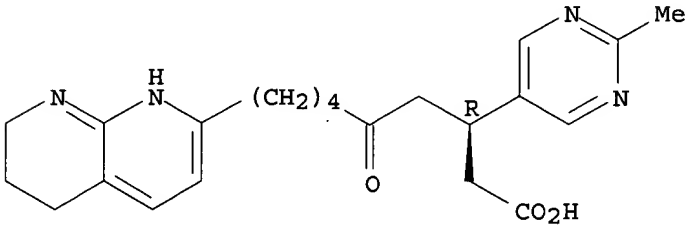
AB The invention discloses novel nonanoic acid derivs. I [X = substituted pyridine, pyrimidine, naphthyridine, etc; R3, R5 = H, OH, alkoxy; R4, R6 = H, alkyl; R3 and R4 or R5 and R6 taken together may form carbonyl oxygen; R7 = (un)substituted Ph, naphthyl, pyridyl, furyl, thienyl, etc.; R8 = H, alkyl] as .alpha.V **integrin** receptor antagonists along with methods for prepn. Thus, compd. II was prepd. in eight steps from 6-oxo-heptanoic acid with chromatog. resoln. of intermediate diketoester racemate. More particularly, the compds. of the present invention are antagonists of the **integrin** receptors .alpha.v.beta.3 and .alpha.v.beta.5, and are useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammation, inflammatory arthritis, viral disease, cancer, and metastatic tumor growth.

IT **312261-73-7P 312261-74-8P 312262-00-3P**
312262-01-4P 312262-03-6P 312262-04-7P
312262-06-9P 312262-07-0P 312262-09-2P
312262-10-5P 312262-12-7P 312262-13-8P
312262-15-0P 312262-16-1P 312262-21-8P
312262-22-9P 312262-24-1P 312262-25-2P
312262-35-4P 312262-36-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study);**

PREP (Preparation); USES (Uses)
(prepn. and biol. activity of nonanoic acid derivs. as .alpha.V **integrin** receptor antagonists)

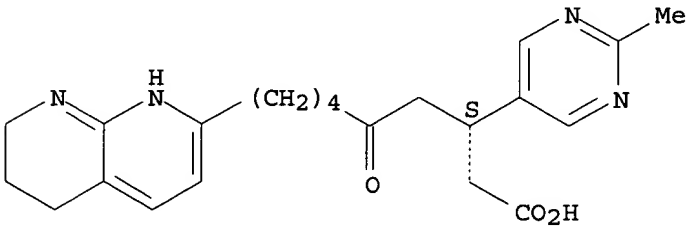
RN 312261-73-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



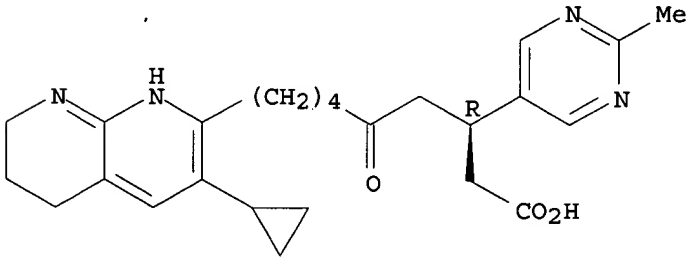
RN 312261-74-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312262-00-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

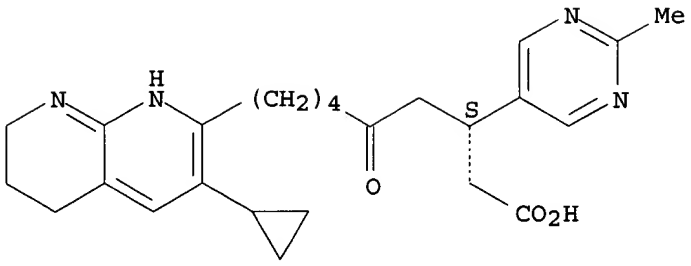
Absolute stereochemistry.



RN 312262-01-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

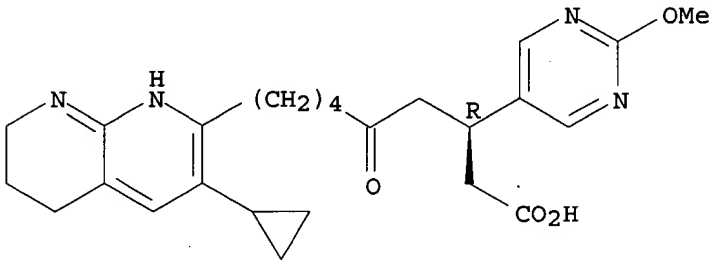
Absolute stereochemistry.

~~09/400,992~~



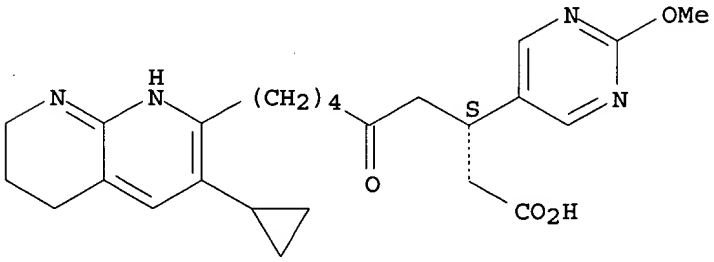
RN 312262-03-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



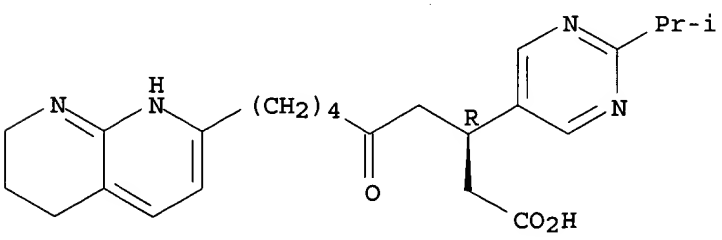
RN 312262-04-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312262-06-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-[2-(1-methylethyl)-5-pyrimidinyl]-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

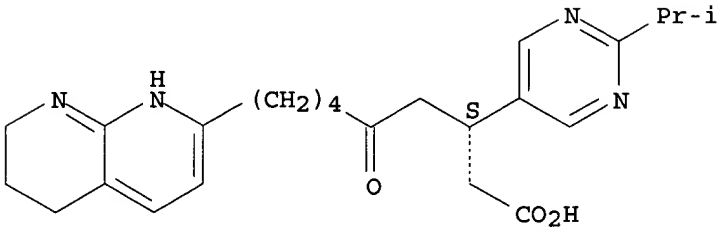
Absolute stereochemistry.



~~09/400,992~~

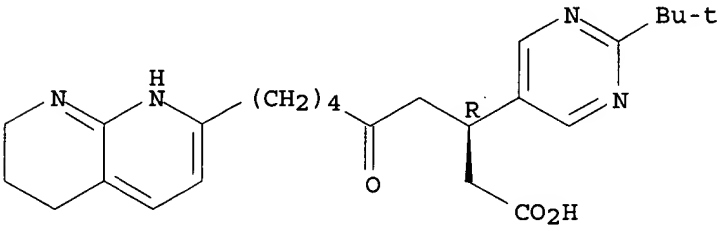
RN 312262-07-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-[2-(1-methylethyl)-5-pyrimidinyl]-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



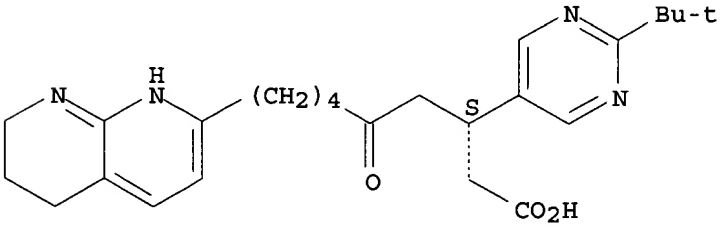
RN 312262-09-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-[2-(1,1-dimethylethyl)-5-pyrimidinyl]-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312262-10-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-[2-(1,1-dimethylethyl)-5-pyrimidinyl]-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

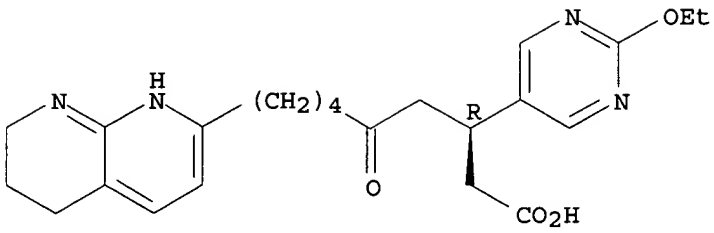
Absolute stereochemistry.



RN 312262-12-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

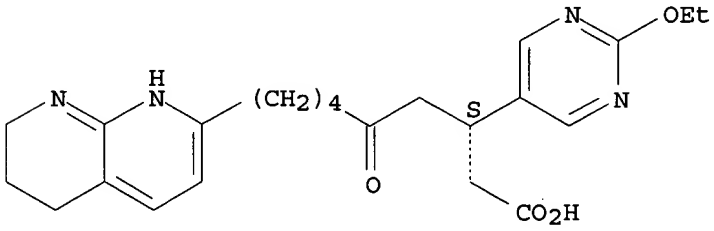
Absolute stereochemistry.

~~09/400,992~~



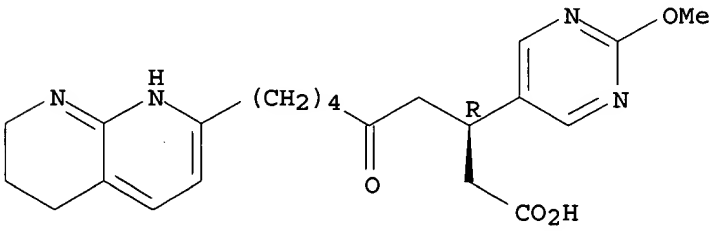
RN 312262-13-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



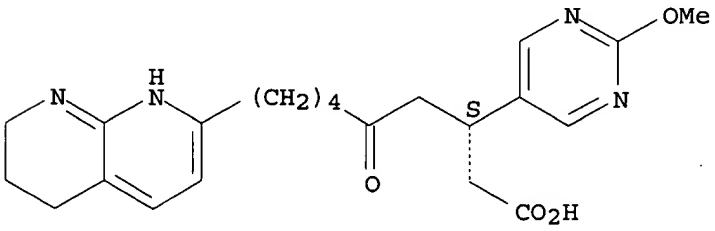
RN 312262-15-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312262-16-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

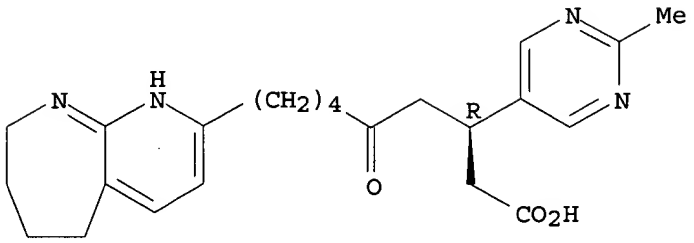
Absolute stereochemistry.



RN 312262-21-8 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

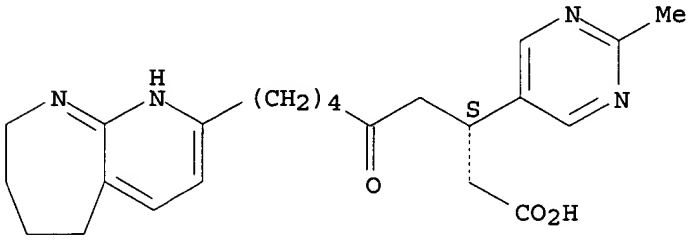
~~09/400,992~~

Absolute stereochemistry.



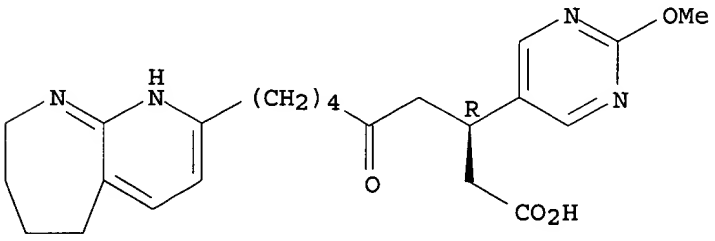
RN 312262-22-9 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



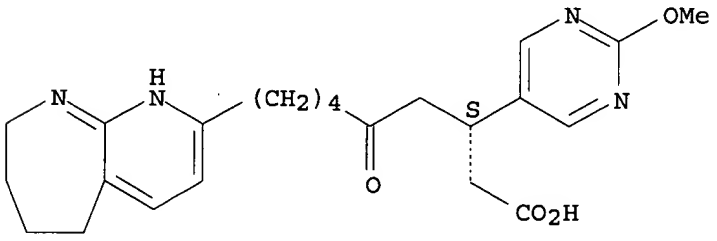
RN 312262-24-1 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



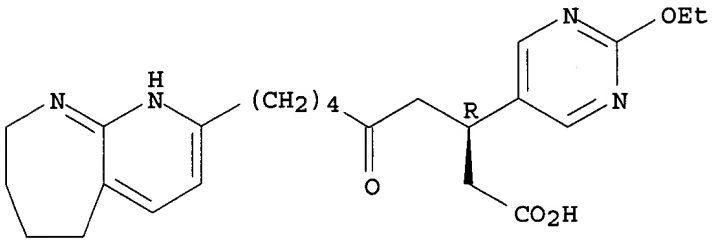
RN 312262-25-2 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



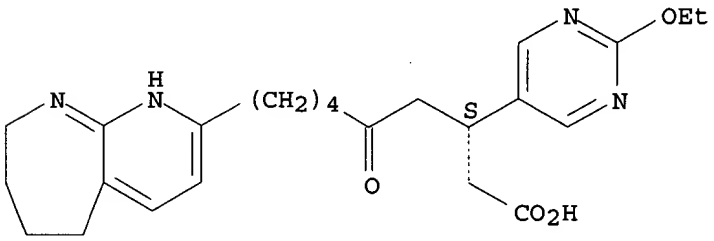
RN 312262-35-4 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-5,6,7,8-tetrahydro-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312262-36-5 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-5,6,7,8-tetrahydro-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **312261-69-1P 312261-70-4P 312261-71-5P**
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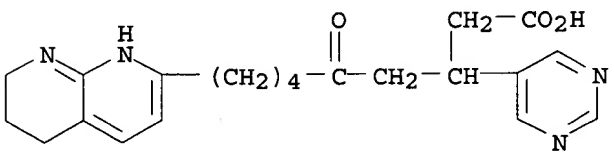
312263-63-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. and biol. activity of nonanoic acid derivs. as .alpha.V **integrin** receptor antagonists)

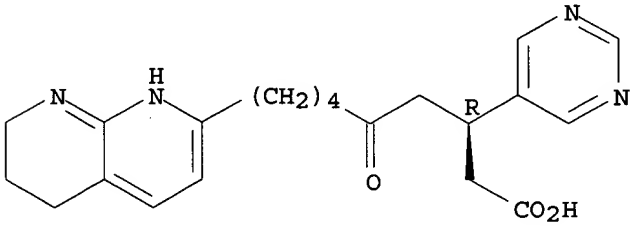
RN 312261-69-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.delta.-oxo-.beta.-5-

pyrimidinyl- (9CI) (CA INDEX NAME)



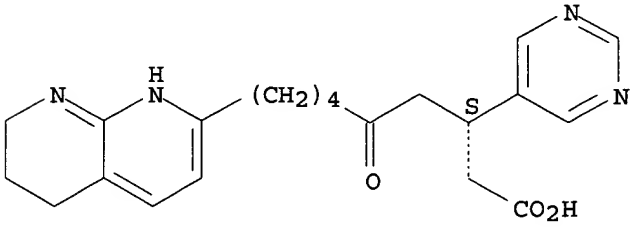
RN 312261-70-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.delta.-oxo-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

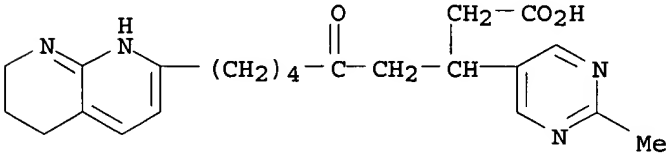


RN 312261-71-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.delta.-oxo-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

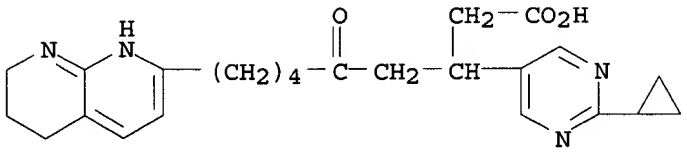
Absolute stereochemistry.



RN 312261-72-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)

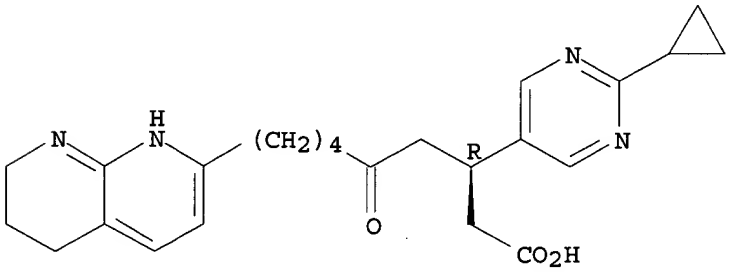


RN 312261-75-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-cyclopropyl-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo- (9CI) (CA INDEX NAME)



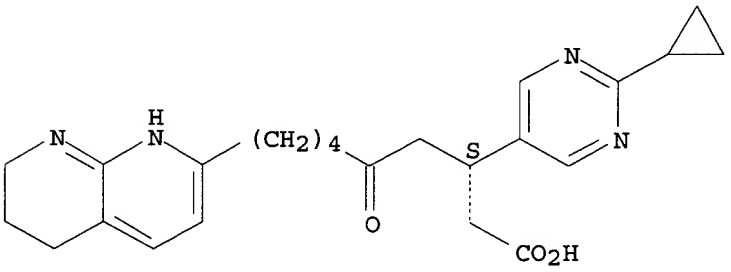
RN 312261-76-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-cyclopropyl-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

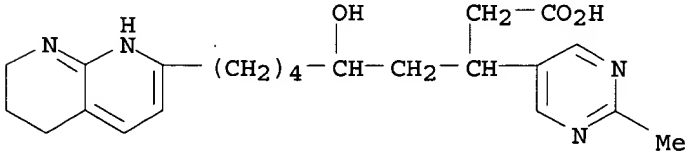


RN 312261-77-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-cyclopropyl-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

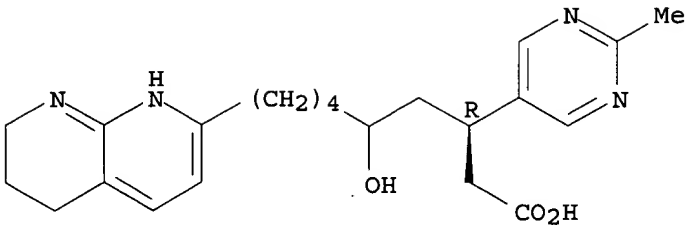


RN 312261-78-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.delta.-hydroxy-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



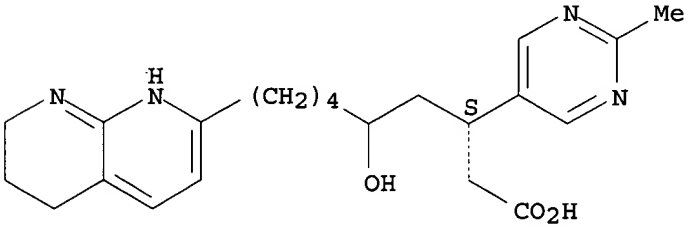
RN 312261-79-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.delta.-hydroxy-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

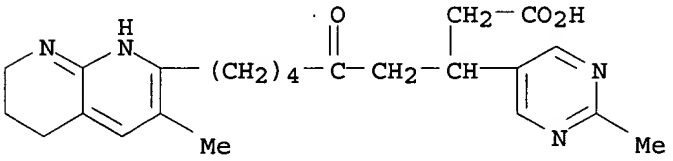


RN 312261-80-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.delta.-hydroxy-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

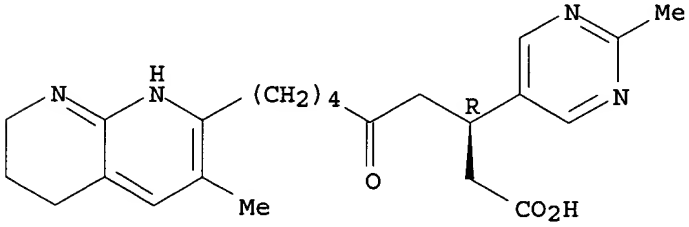


RN 312261-81-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-3-methyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



RN 312261-82-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-3-methyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

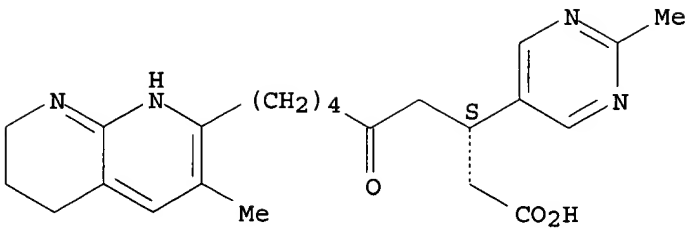
Absolute stereochemistry.



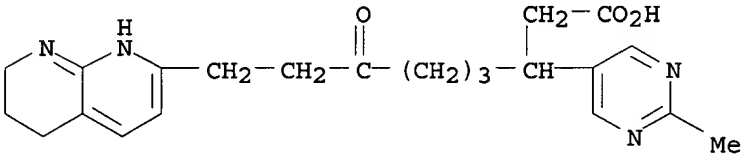
RN 312261-83-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-3-methyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~

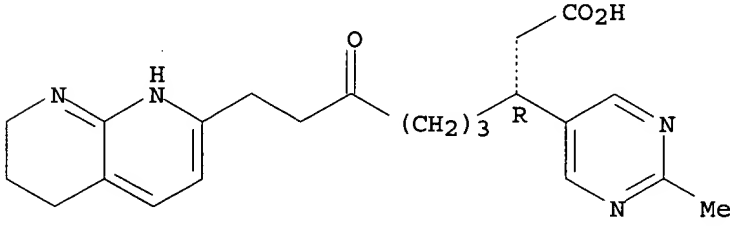


RN 312261-84-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.zeta.-oxo- (9CI) (CA INDEX NAME)



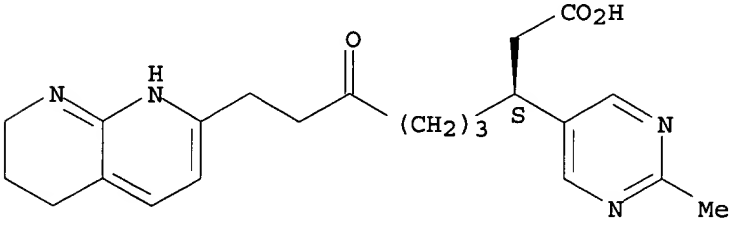
RN 312261-85-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.zeta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

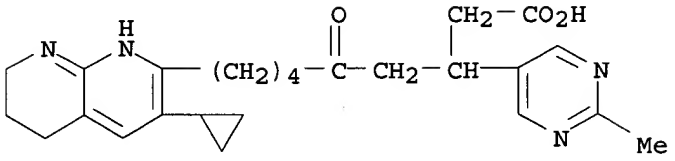


RN 312261-86-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.zeta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

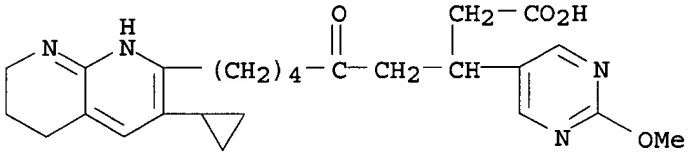
Absolute stereochemistry.



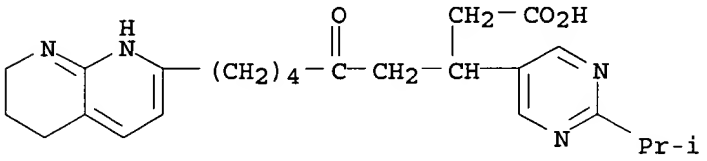
RN 312261-99-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



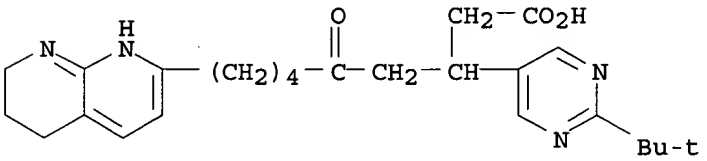
RN 312262-02-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



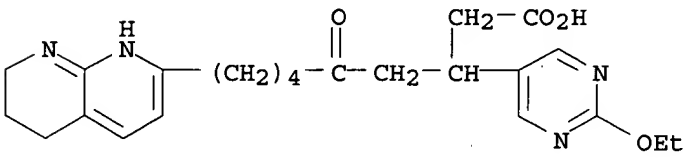
RN 312262-05-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-[2-(1-methylethyl)-5-pyrimidinyl]-.delta.-oxo- (9CI) (CA INDEX NAME)



RN 312262-08-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-[2-(1,1-dimethylethyl)-5-pyrimidinyl]-1,5,6,7-tetrahydro-.delta.-oxo- (9CI) (CA INDEX NAME)

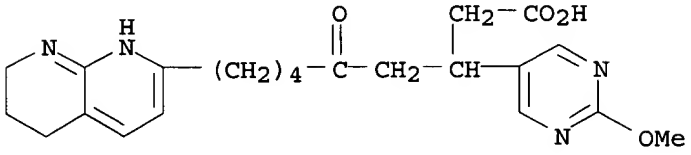


RN 312262-11-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo- (9CI) (CA INDEX NAME)

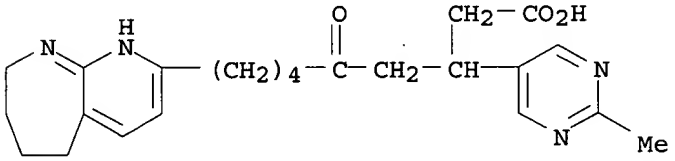


RN 312262-14-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-

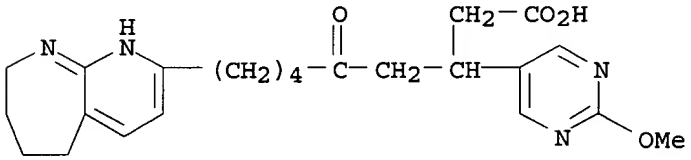
pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



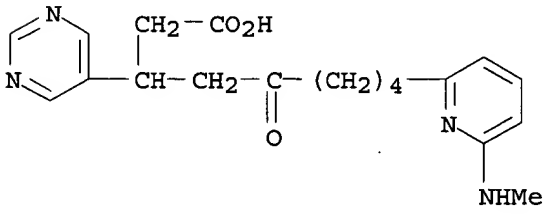
RN 312262-20-7 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



RN 312262-23-0 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



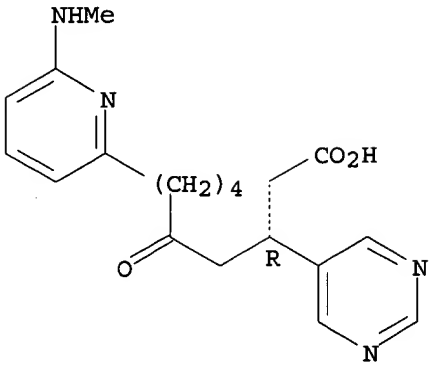
RN 312262-29-6 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]-2-oxohexyl]- (9CI) (CA INDEX NAME)



RN 312262-30-9 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]-2-oxohexyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

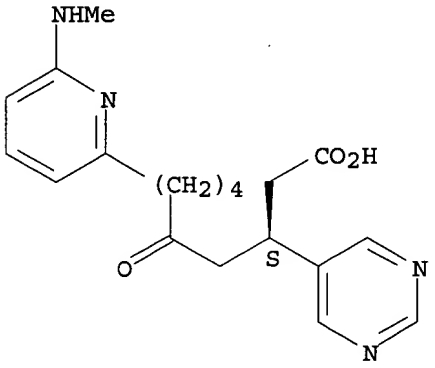
Absolute stereochemistry.

~~09/ 400,992~~

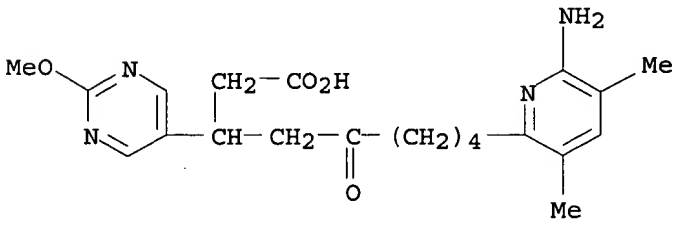


RN 312262-31-0 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]-2-oxohexyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

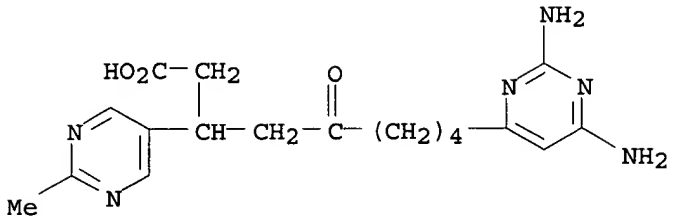
Absolute stereochemistry.



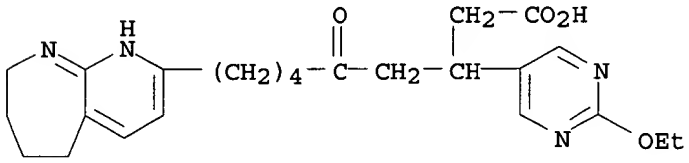
RN 312262-32-1 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[6-(6-amino-3,5-dimethyl-2-pyridinyl)-2-oxohexyl]-2-methoxy- (9CI) (CA INDEX NAME)



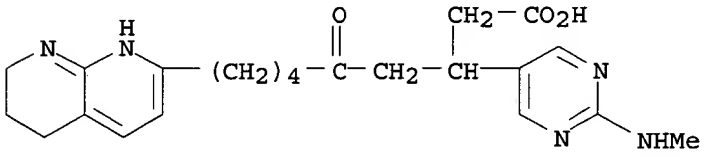
RN 312262-33-2 CAPLUS
CN 4-Pyrimidinenonanoic acid, 2,6-diamino-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



RN 312262-34-3 CAPLUS
CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, .beta.-(2-ethoxy-5-pyrimidinyl)-5,6,7,8-tetrahydro-.delta.-oxo- (9CI) (CA INDEX NAME)

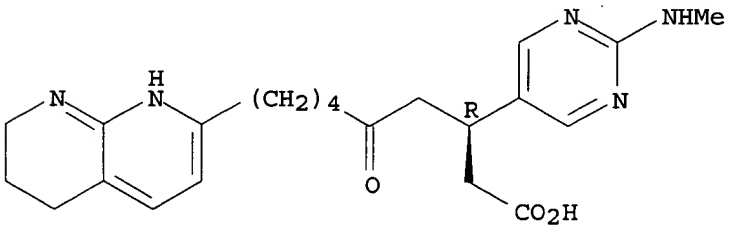


RN 312262-46-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-[2-(methylamino)-5-pyrimidinyl]-.delta.-oxo- (9CI) (CA INDEX NAME)



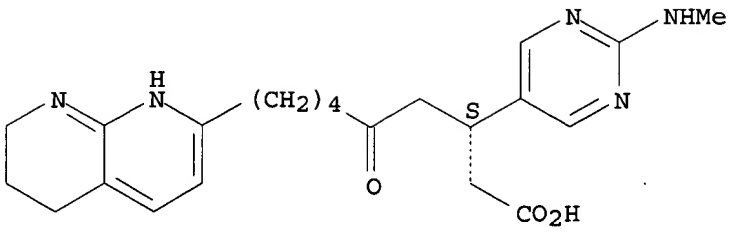
RN 312262-47-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-[2-(methylamino)-5-pyrimidinyl]-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

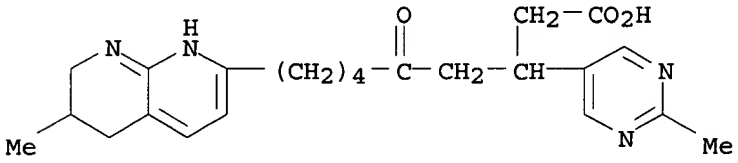


RN 312262-48-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-[2-(methylamino)-5-pyrimidinyl]-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

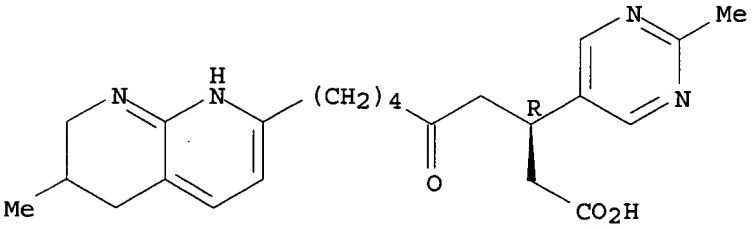


RN 312262-52-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-6-methyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



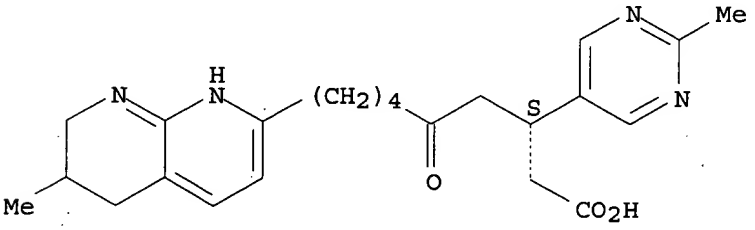
RN 312262-53-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-6-methyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



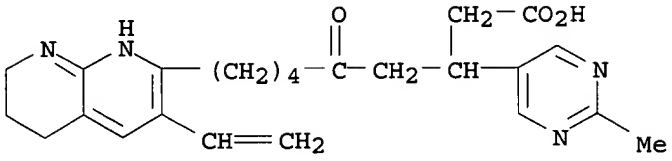
RN 312262-54-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-6-methyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



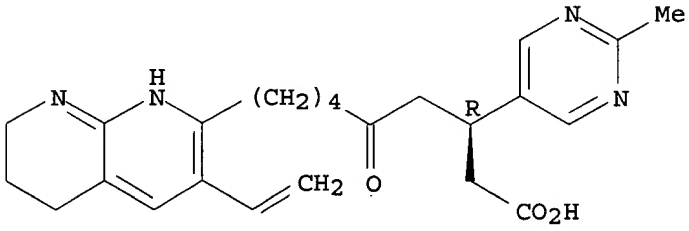
RN 312262-61-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-ethenyl-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)

~~09/ 400,992~~



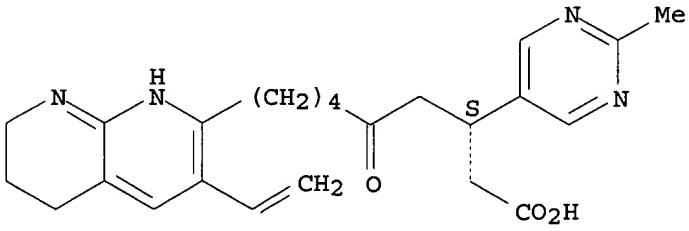
RN 312262-62-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-ethenyl-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

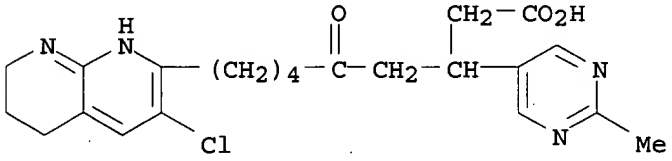


RN 312262-63-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-ethenyl-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

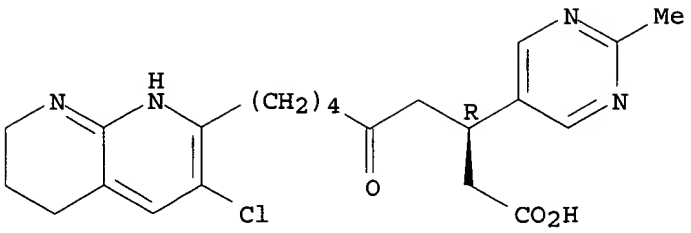


RN 312262-64-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-chloro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



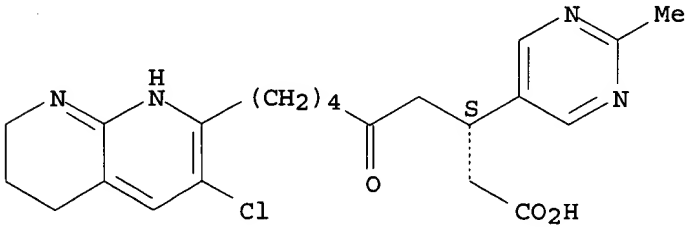
RN 312262-65-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-chloro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

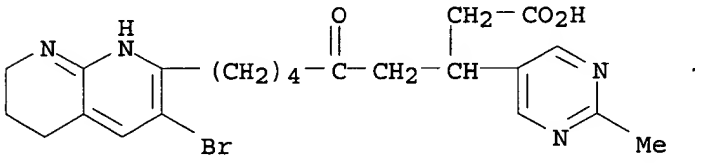


RN 312262-66-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-chloro-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

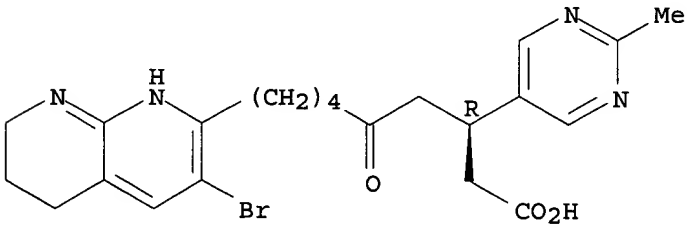


RN 312262-67-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-bromo-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



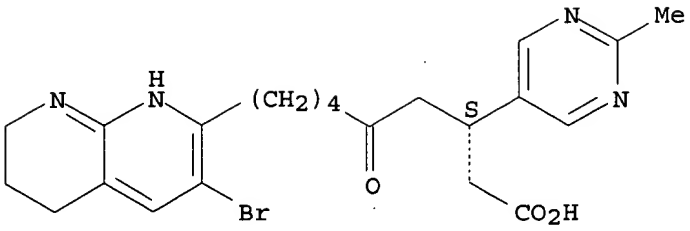
RN 312262-68-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-bromo-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

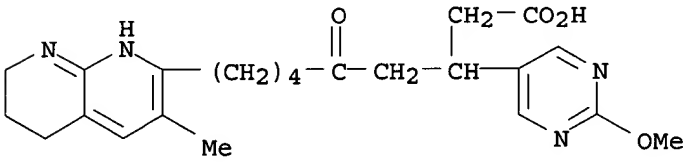


RN 312262-69-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-bromo-1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

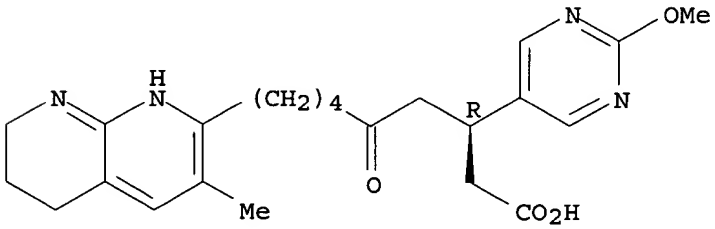


RN 312262-70-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-3-methyl-.delta.-oxo- (9CI) (CA INDEX NAME)



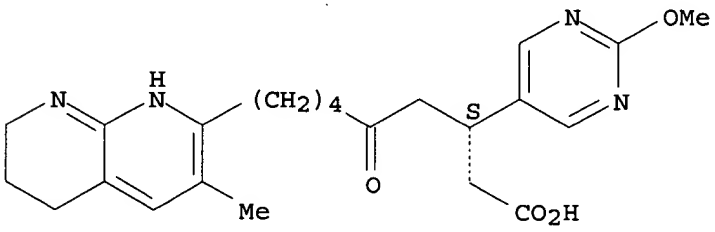
RN 312262-71-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-3-methyl-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

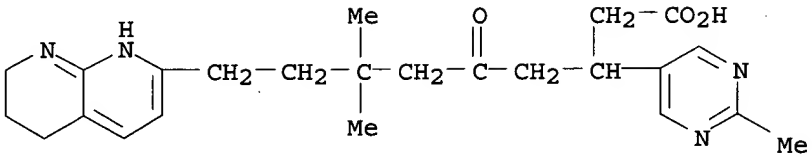


RN 312262-72-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-3-methyl-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

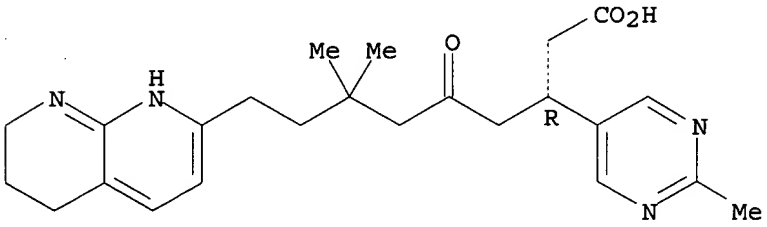


RN 312262-76-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.zeta.,.zeta.-dimethyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo- (9CI) (CA INDEX NAME)



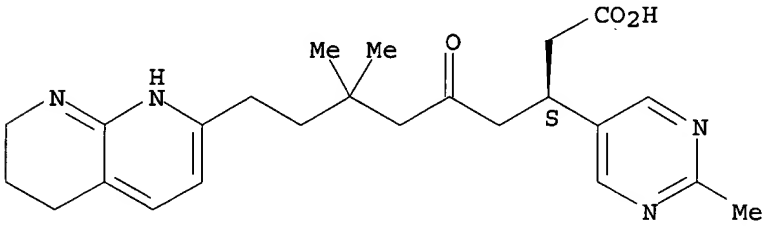
RN 312262-77-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.zeta.,.zeta.-dimethyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

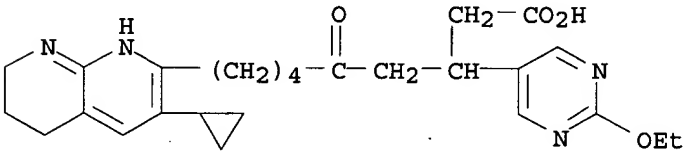


RN 312262-78-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.zeta.,.zeta.-dimethyl-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

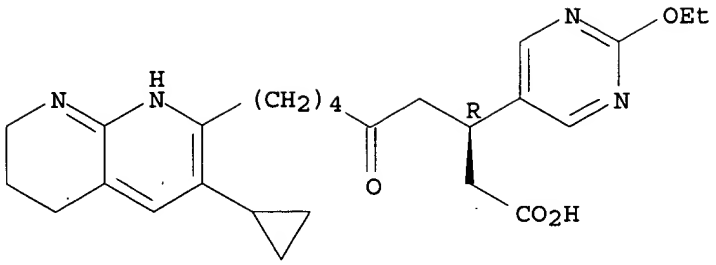


RN 312262-79-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-.beta.-(2-ethoxy-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo- (9CI) (CA INDEX NAME)



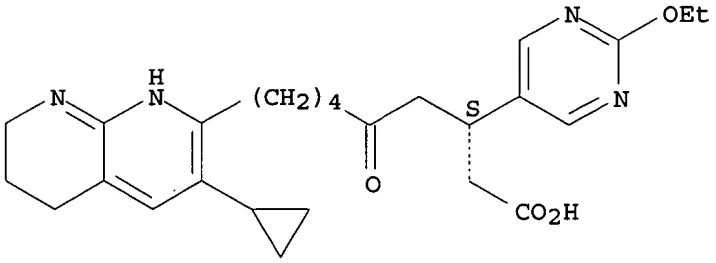
RN 312262-80-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-.beta.-(2-ethoxy-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

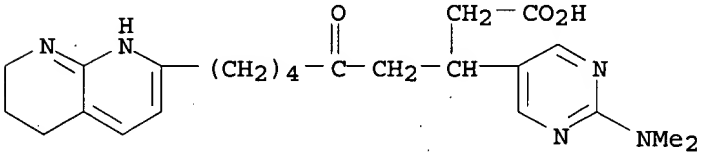


RN 312262-81-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-.beta.-(2-ethoxy-5-pyrimidinyl)-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

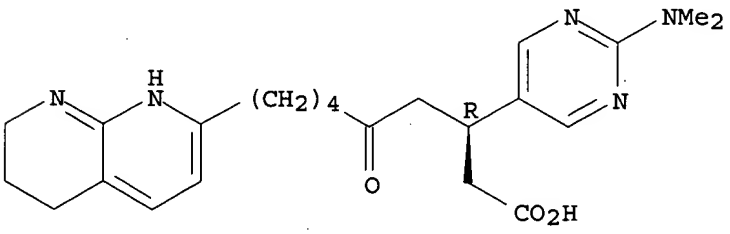


RN 312262-85-4 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-[2-(dimethylamino)-5-pyrimidinyl]-1,5,6,7-tetrahydro-.delta.-oxo- (9CI) (CA INDEX NAME)



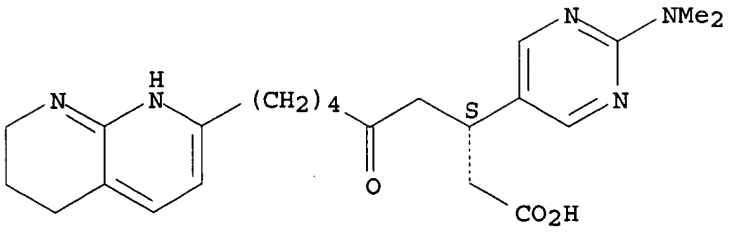
RN 312262-86-5 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-[2-(dimethylamino)-5-pyrimidinyl]-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



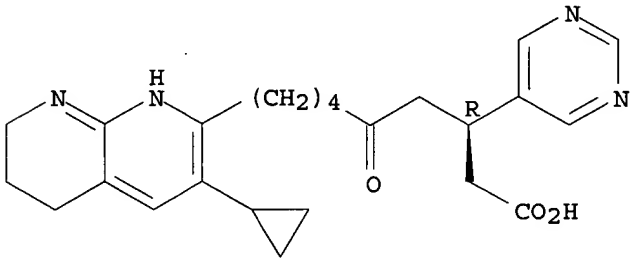
RN 312262-87-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, .beta.-[2-(dimethylamino)-5-pyrimidinyl]-1,5,6,7-tetrahydro-.delta.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



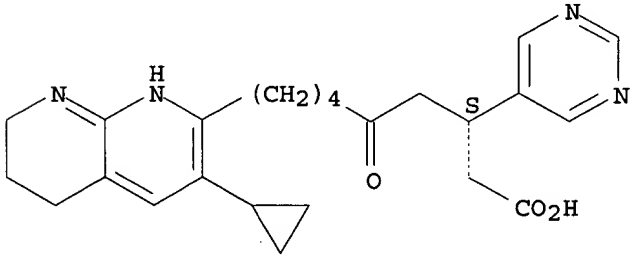
RN 312262-88-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.delta.-oxo-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 312262-89-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 3-cyclopropyl-1,5,6,7-tetrahydro-.delta.-oxo-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



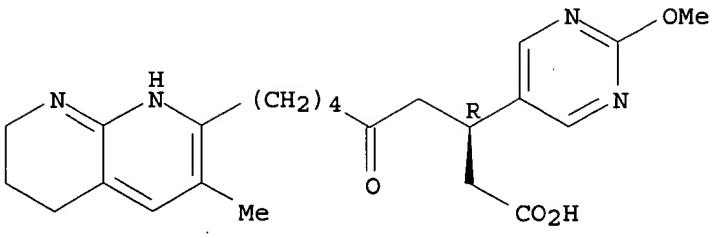
RN 312263-62-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-3-methyl-.delta.-oxo-, (.beta.R)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 312262-71-8
CMF C23 H30 N4 O4

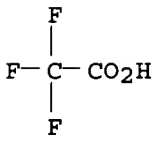
Absolute stereochemistry.

09/400,982



CM 2

CRN 76-05-1
CMF C2 H F3 O2

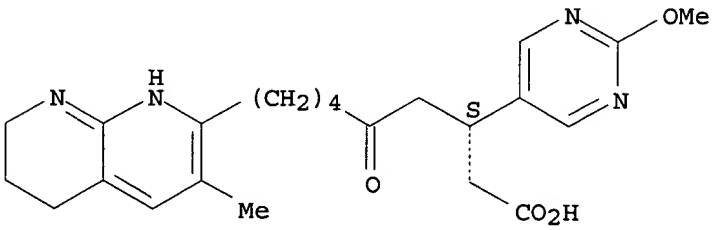


RN 312263-63-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-3-methyl-.delta.-oxo-, (.beta.S)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

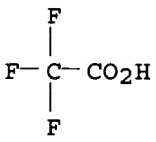
CRN 312262-72-9
CMF C23 H30 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L7 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS

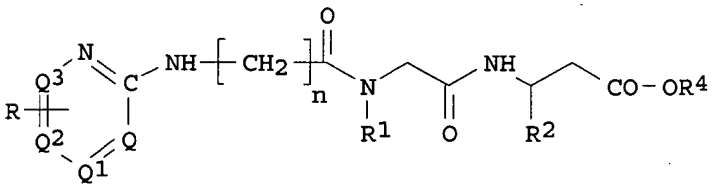
~~09/400,992~~

ACCESSION NUMBER: 2000:592698 CAPLUS
DOCUMENT NUMBER: 133:164332
TITLE: Preparation of .beta.-alanine derivatives for use as **integrin** inhibitors
INVENTOR(S): Holzemann, Gunter; Goodman, Simon; Jonczyk, Alfred; Stahle, Wolfgang
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048996	A2	20000824	WO 2000-EP969	20000208
WO 2000048996	A3	20001116		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1153014	A2	20011114	EP 2000-909151	20000208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008310	A	20020122	BR 2000-8310	20000208
JP 2002537287	T2	20021105	JP 2000-599737	20000208
NO 2001004010	A	20011018	NO 2001-4010	20010817

PRIORITY APPLN. INFO.: DE 1999-19907370 A 19990220
DE 1999-19957787 A 19991201
WO 2000-EP969 W 20000208

OTHER SOURCE(S): MARPAT 133:164332
GI

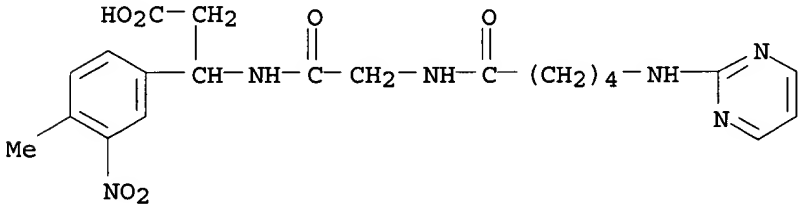


I

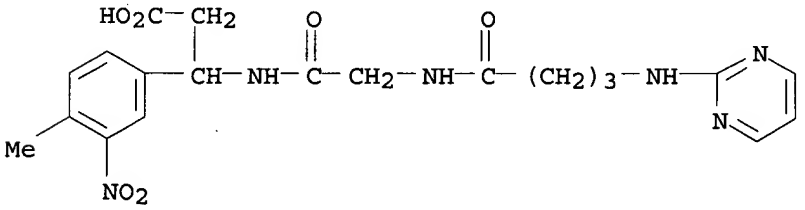
AB The invention relates to novel .beta.-alanine derivs. [(I); Q, Q1, Q2, Q3 = CH, N; R = H, alkyl, aryl, halogen, OH, alkoxy, CF3, OCF3; R1 = H, alkyl; R2 = substituted phenyl; R3 = H, alkyl, halogen, OH, alkoxy, CF3, OCF3, CN, NH2, (di)alkyl amine, alkyl amide; R4 = H, (hydroxy)alkyl, alkyl ester, (un)substituted aralkyl; n = 2-6] and to their physiol. acceptable salts or solvates, useful in the treatment of diseases as selective .alpha.v.beta.3-, .alpha.v.beta.5-, or .alpha.v.beta.6-**integrin** inhibitors. Thus, 4-(trifluoromethoxy)-benzaldehyde, malonic acid, and ammonium acetate were reacted, and the product 3-amino-3-(4-trifluoromethoxyphenyl)propionic acid was esterified with thionyl chloride and methanol to give II. Glycine Me ester was condensed with 4-(4-methylpyridin-2-ylamino)butyric acid and the deesterified product reacted with II to give I [Q, Q1, Q2, Q3 = CH; R, R1 = H; R2 =

4-F3CO-C6H4; R4 = Me; n = 3], which was deesterified to the free propionic acid deriv. and converted to the sodium or trifluoroacetate salts. Title compds. can be used in the treatment of thrombosis, heart infarct, coronary heart diseases, arteriosclerosis, inflammations, tumors, osteoporosis, infections and restenosis after angioplasty or in pathol. processes induced or propagated by angiogenesis. Title compds. were tested for **integrin** inhibition in vivo in mice (no data).

IT **287965-36-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **BIOL (Biological study)**
(prepn. of .beta.-alanine derivs. for use as **integrin** inhibitors)
RN 287965-36-0 CAPLUS
CN .beta.-Alanine, N-[1-oxo-5-(2-pyrimidinylamino)pentyl]glycyl-3-(4-methyl-3-nitrophenyl)- (9CI) (CA INDEX NAME)



IT **287965-31-5P 287965-32-6P 287965-33-7P**
287965-34-8P 287965-35-9P 287966-66-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation)
(prepn. of .beta.-alanine derivs. for use as **integrin** inhibitors)
RN 287965-31-5 CAPLUS
CN .beta.-Alanine, N-[1-oxo-4-(2-pyrimidinylamino)butyl]glycyl-3-(4-methyl-3-nitrophenyl)- (9CI) (CA INDEX NAME)

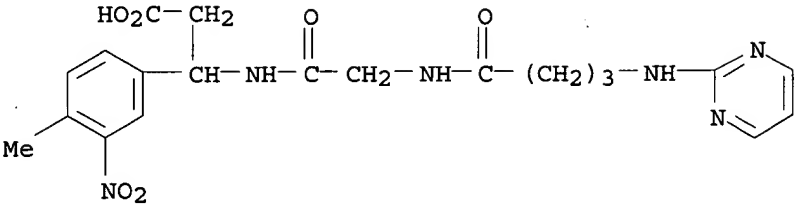


RN 287965-32-6 CAPLUS
CN .beta.-Alanine, N-[1-oxo-4-(2-pyrimidinylamino)butyl]glycyl-3-(4-methyl-3-nitrophenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

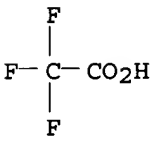
CRN 287965-31-5
CMF C20 H24 N6 O6

~~09/400,992~~

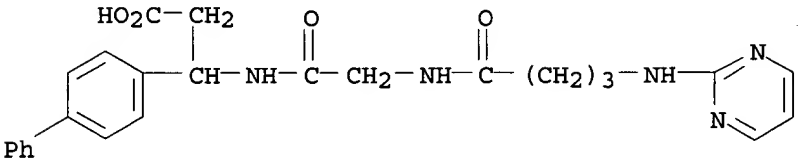


CM 2

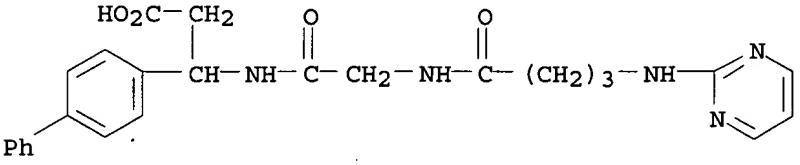
CRN 76-05-1
CMF C2 H F3 O2



RN 287965-33-7 CAPLUS
CN .beta.-Alanine, N-[1-oxo-4-(2-pyrimidinylamino)butyl]glycyl-3-[1,1'-biphenyl]-4-yl- (9CI) (CA INDEX NAME)



RN 287965-34-8 CAPLUS
CN .beta.-Alanine, N-[1-oxo-4-(2-pyrimidinylamino)butyl]glycyl-3-[1,1'-biphenyl]-4-yl-, monosodium salt (9CI) (CA INDEX NAME)



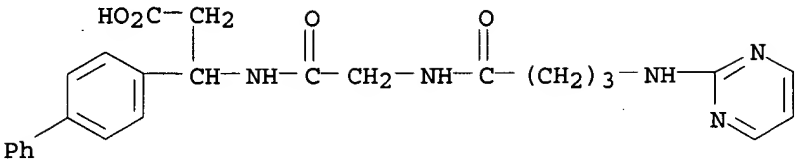
● Na

RN 287965-35-9 CAPLUS
CN .beta.-Alanine, N-[1-oxo-4-(2-pyrimidinylamino)butyl]glycyl-3-[1,1'-biphenyl]-4-yl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

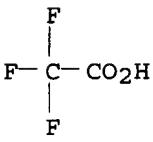
CRN 287965-33-7
CMF C25 H27 N5 O4

~~09/ 400,992~~

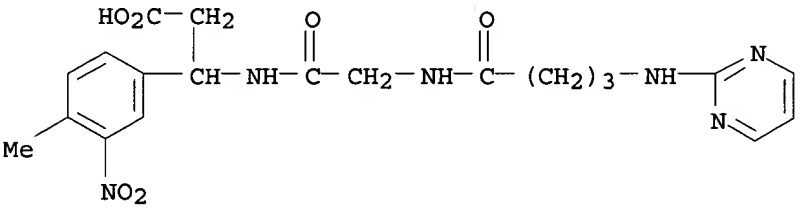


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 287966-66-9 CAPLUS
CN .beta.-Alanine, N-[1-oxo-4-(2-pyrimidinylamino)butyl]glycyl-3-(4-methyl-3-nitrophenyl)-, monosodium salt (9CI) (CA INDEX NAME)



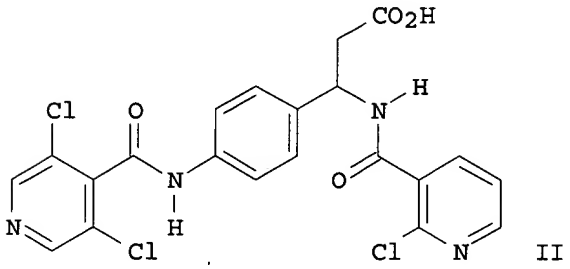
● Na

L7 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:384156 CAPLUS
DOCUMENT NUMBER: 133:30662
TITLE: Preparation of N-heteroaroyl-.beta.-alanines as .alpha.4 **integrin** inhibitors
INVENTOR(S): Porter, John Robert; Head, John Clifford; Warrellow, Graham John; Archibald, Sarah Catherine
PATENT ASSIGNEE(S): Celltech Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032575	A1	20000608	WO 1999-GB3986	19991129

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1135371 A1 20010926 EP 1999-973020 19991129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
JP 2002531439 T2 20020924 JP 2000-585217 19991129
PRIORITY APPLN. INFO.: GB 1998-26174 A 19981130
WO 1999-GB3986 W 19991129
OTHER SOURCE(S): MARPAT 133:30662
GI



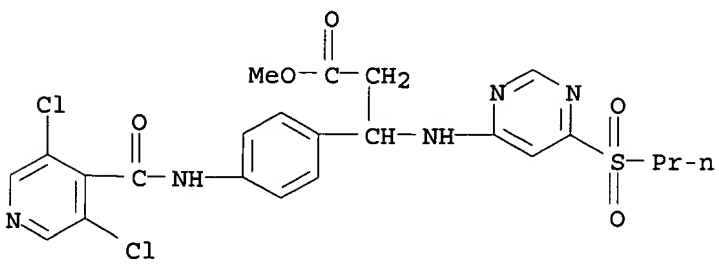
II

AB R4ZZ1Z2CHR1CRR5R6 [I; R = (un)derivatized CO2H; R1 = NHR3, NHSO2R3, NHCOR3, etc.; R3 = aliph. group, (hetero)aryl, etc.; R4 = (un)substituted (hetero)aryl; R5,R6 = H, halo, alkyl, alkoxy, etc.,; Z = bond, (un)substituted (hetero)aliph. chain (sic); Z1 = bond, O, (alkyl)imino, CONH, CO2H, etc.; Z2 = (un)substituted phenylene, pyridinediyl, pyrazinediyl, etc.] were prepd. Thus, 4-(H2N)C6H4CH(NHCO2CMe3)CH2CO2Me (prepn. given) was amidated by 3,5-dichloroisonicotinoyl chloride and the deprotected product amidated by 2-chloronicotinic acid to give, after sapon., title compd. II. Data for biol. activity of I were given.

IT **273919-77-0P 273919-78-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of N-heteroaroyl-.beta.-alanines as .alpha.4 **integrin** inhibitors)

RN 273919-77-0 CAPLUS

CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.beta.-[[6-(propylsulfonyl)-4-pyrimidinyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



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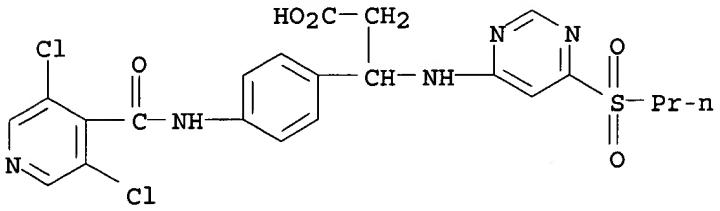
RN 273919-78-1 CAPLUS
CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.beta.-[[6-(propylsulfonyl)-4-pyrimidinyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:260225 CAPLUS
DOCUMENT NUMBER: 132:294010
TITLE: Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors
INVENTOR(S): Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021920	A1	20000420	WO 1999-EP7620	19991012
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6331640	B1	20011218	US 1999-407534	19990929
CA 2344058	AA	20000420	CA 1999-2344058	19991012
BR 9914602	A	20010703	BR 1999-14602	19991012
EP 1121342	A1	20010808	EP 1999-953772	19991012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527416	T2	20020827	JP 2000-575829	19991012
US 2002052512	A1	20020502	US 2001-879700	20010612

PRIORITY APPLN. INFO.: US 1998-104120P P 19981013
US 1999-407534 A3 19990929
WO 1999-EP7620 W 19991012
OTHER SOURCE(S): MARPAT 132:294010
GI

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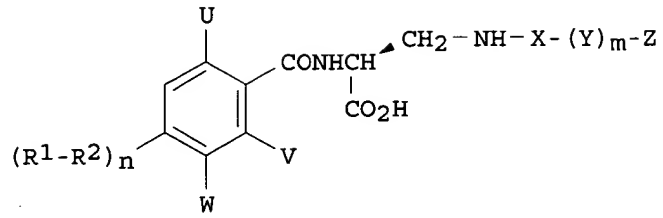


I

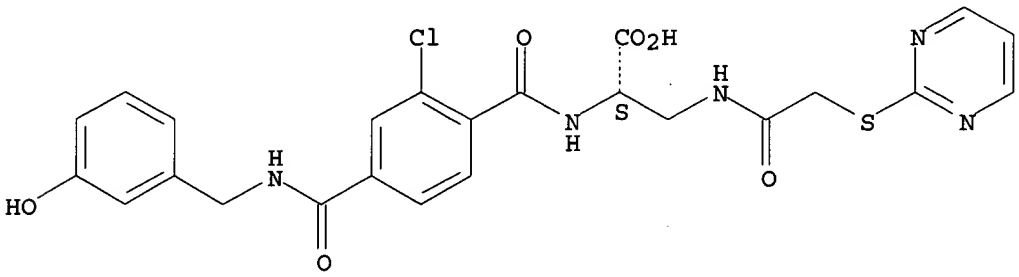
AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkylenethio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepd. and are useful for treating rheumatoid arthritis, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of ischemia reperfusion injury, including acute myocardial infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepd. by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-assocd. antigen-1)/ICAM-1 protein-protein assay.

IT **264273-37-2P 264274-10-4P 264274-11-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264273-37-2 CAPLUS

CN L-Alanine, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-[[(2-pyrimidinylthio)acetyl]amino]- (9CI) (CA INDEX NAME)

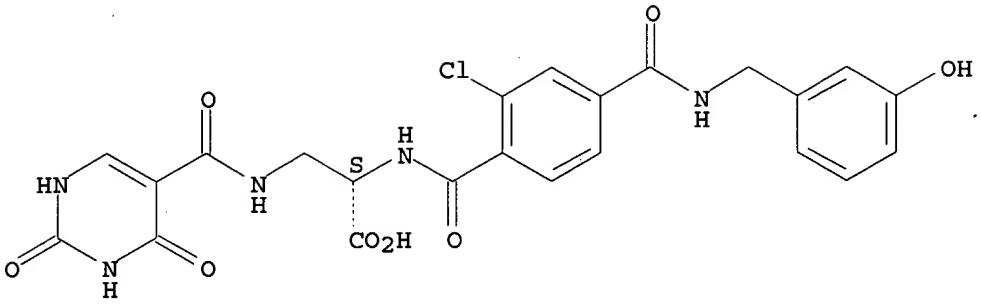
Absolute stereochemistry.



RN 264274-10-4 CAPLUS

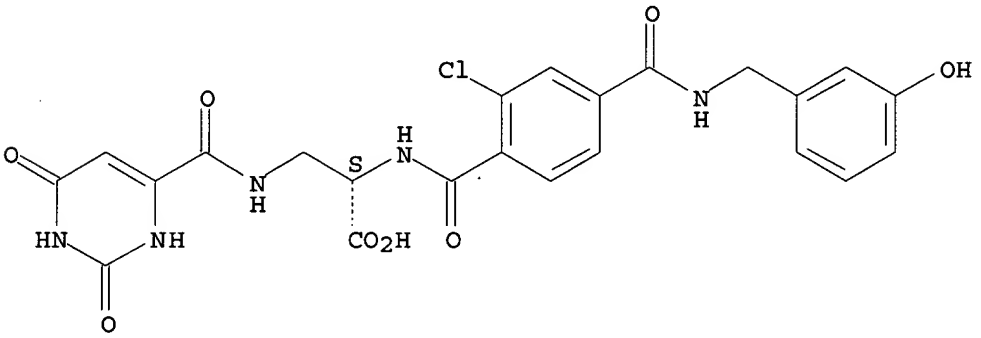
CN L-Alanine, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 264274-11-5 CAPLUS
CN L-Alanine, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-[[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:227650 CAPLUS
DOCUMENT NUMBER: 132:265501
TITLE: Phenylalanine derivatives as alpha 4 **integrin** inhibitors
INVENTOR(S): Head, John Clifford; Porter, John Robert; Warrellow, Graham John; Archibald, Sarah Catherine; Hutchinson, Brian Woodside
PATENT ASSIGNEE(S): Celltech Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018759	A1	20000406	WO 1999-GB3210	19990928

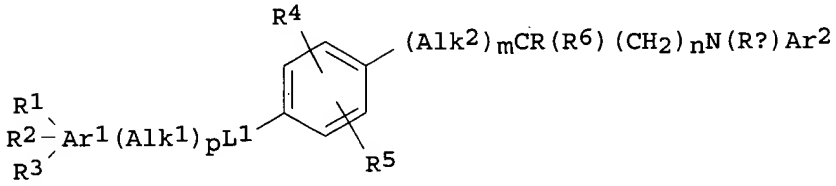
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

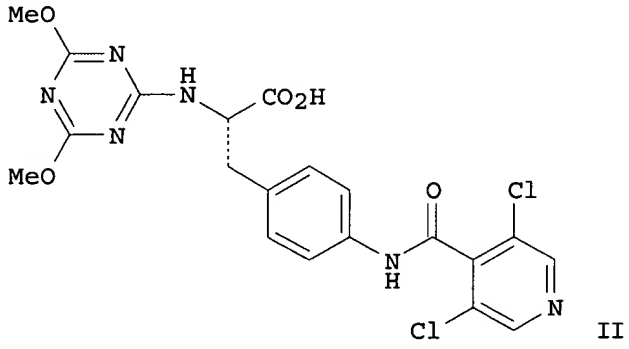
US 6348463	B1	20020219	US 1999-406560	19990927	
CA 2338442	AA	20000406	CA 1999-2338442	19990928	
AU 9961059	A1	20000417	AU 1999-61059	19990928	
EP 1117657	A1	20010725	EP 1999-947680	19990928	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002525367	T2	20020813	JP 2000-572219	19990928	
US 2002028812	A1	20020307	US 2001-927874	20010810	
PRIORITY APPLN. INFO.:			GB 1998-21061	A	19980928
			US 1999-406560	A3	19990927
			WO 1999-GB3210	W	19990928

OTHER SOURCE(S): MARPAT 132:265501

GI



I



II

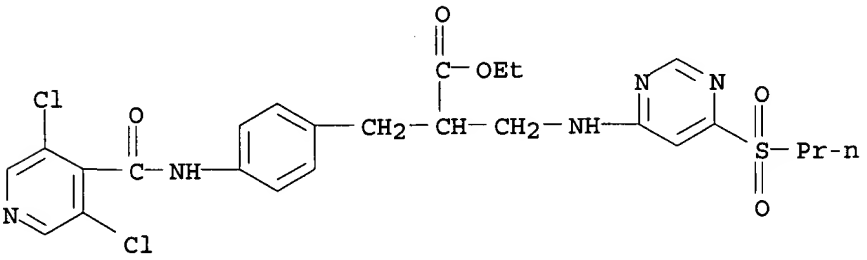
AB Phenylalanine derivs. I [Ar1 = arom. or heteroarom. group; Alk1 = (un)substituted aliph. or heteroaliph. chain; L1, L2, L3 = a covalent bond or a linker atom or group; Alk2 = alkylene; R is a carboxylic acid or deriv.; Ar2 = (un)substituted arom. or heteroarom. group; R1, R2, R3, R4, R5 = -L2(Alk3)tL3(R7)u; Alk3 = aliph. or heteroaliph. chain; R6, Ra = H, Me; R7 = H, halo, alkyl, OH, SH, NH2, (un)substituted alkoxy, thioalkyl, or aminoalkyl; m, n, p, t = 0, 1; u = 1-3] and their salts, solvates, hydrates, and N-oxides were prepd. as selective inhibitors of .alpha.4 **integrins** useful for the prophylaxis and treatment of immune or inflammatory disorders. For example, a multi-step synthesis of the title compd. II was given. Compds. I were tested for inhibition of **integrin**-dependent cell adhesion and generally have IC50 values of .ltoreq. 1.mu.M in .alpha.4.beta.1 and .alpha.4.beta.7 assays, and IC50 values of .gtoreq. 50 .mu.M in assays of other **integrins**.

IT **263275-13-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of phenylalanine derivs. as alpha 4 **integrin** inhibitors)

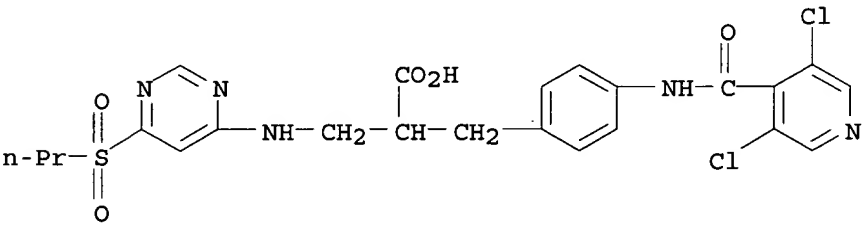
RN 263275-13-4 CAPLUS

~~09/ 400,992~~

CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.alpha.-[[[6-(propylsulfonyl)-4-pyrimidinyl]amino]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **263275-14-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of phenylalanine derivs. as alpha 4 **integrin** inhibitors)
RN 263275-14-5 CAPLUS
CN Benzenepropanoic acid, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-.alpha.-[[[6-(propylsulfonyl)-4-pyrimidinyl]amino]methyl]- (9CI) (CA INDEX NAME)



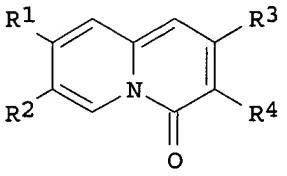
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:210162 CAPLUS
DOCUMENT NUMBER: 132:237000
TITLE: Quinolizinones as **integrin** inhibitors
INVENTOR(S): Lamothe, Serge; Zacharie, Boulos; Attardo, Giorgio; Labrecque, Denis; Courchesne, Marc; Falardeau, Guy; Rej, Rabindra; Abbott, Shaun
PATENT ASSIGNEE(S): Biochem Pharma, Inc., Can.
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

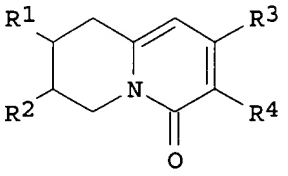
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017197	A1	20000330	WO 1999-IB1564	19990921

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,

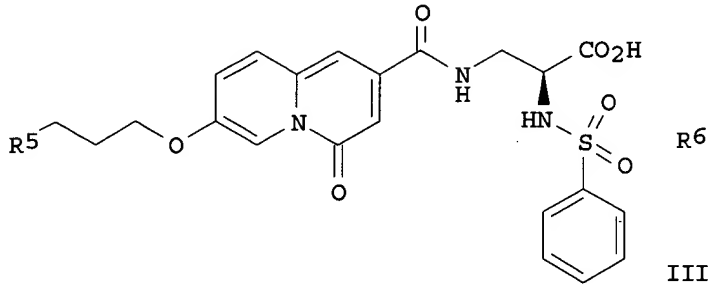
SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9959916 A1 20000410 AU 1999-59916 19990921
EP 1115724 A1 20010718 EP 1999-969413 19990921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1998-101257P P 19980921
WO 1999-IB1564 W 19990921
OTHER SOURCE(S): MARPAT 132:237000
GI



I



II



III

AB The quinolizinone (I) and tetrahydroquinolizinone analogs (II) (one of R1 and R2 = -J-K-L and other H ;(J = -(CH2)m-, -(CH2)mQ(CH2)n; K, L = (un)substituted alkyl,cycloalkyl, aryl, alkenyl etc); one of R3 and R4 = -X-Y-Z and other H (X,Y = -(CH2)m-, -(CH2)mQ(CH2)n; Z = H, CO2H, CO2R and SO2R, R = alkyl, cycloalkyl etc.) (Q = O, S, amino, CO2, etc.))where m, n, o and p are independently integer from 0-6, and their pharmaceutically acceptable salts, solvates or metabolic precursors were prepd. as effective inhibitors of **integrins**, particularly .alpha.IIb.beta.3 or .alpha.v **integrins** such as .alpha.v.beta.3 and .alpha.v.beta.5. Thus, compd. (III) (R5 = NHC(=NH)NH2, R6 = HCl) was prepd. by benzylation of 6-methyl-pyridin-3-ol followed by acetoxylation, oxidn., condensation with 2-(diethoxy-phosphoryl)-succinic acid di-Me ester, debenzylation, alkylation with 3-iodopropyl-carbamic acid tert-Bu ester, deesterification, condensation with (S)-3-amino-2-benzenesulfonylamino-propionic acid, treatment with trifluoroacetic acid and reacting trifluoroacetic acid salt of III (R5 = NH2, R6 = CF3CO2H) with 1H-pyrazole-1-carboxamidine hydrochloride. The IC50 of III for **integrins** .alpha.v.beta.3 and .alpha.IIb.beta.3 in fibrinogen binding assay was 0.015 and 0.0053.mu.M.

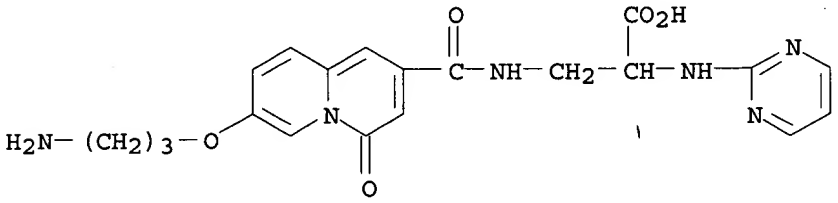
IT **262277-61-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation);

~~09/400,992~~

RACT (Reactant or reagent); USES (Uses)
(quinolizinones as **integrin** inhibitors)

RN 262277-61-2 CAPLUS

CN Alanine, 3-[[[7-(3-aminopropoxy)-4-oxo-4H-quinolizin-2-yl]carbonyl]amino]-N-2-pyrimidinyl-, monohydrochloride (9CI) (CA INDEX NAME)

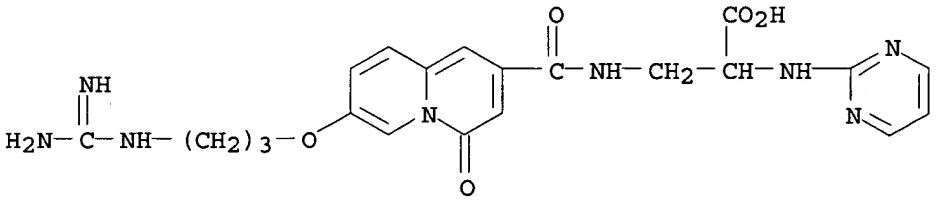


● HCl

IT **262277-62-3P 262277-66-7P 262277-96-3P**
262277-99-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(quinolizinones as **integrin** inhibitors)

RN 262277-62-3 CAPLUS

CN Alanine, 3-[[[7-[3-[(aminoiminomethyl)amino]propoxy]-4-oxo-4H-quinolizin-2-yl]carbonyl]amino]-N-2-pyrimidinyl-, dihydrochloride (9CI) (CA INDEX NAME)

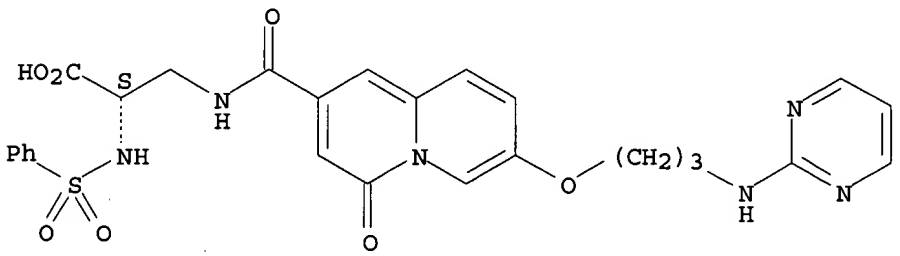


●2 HCl

RN 262277-66-7 CAPLUS

CN L-Alanine, 3-[[[4-oxo-7-[3-(2-pyrimidinylamino)propoxy]-4H-quinolizin-2-yl]carbonyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



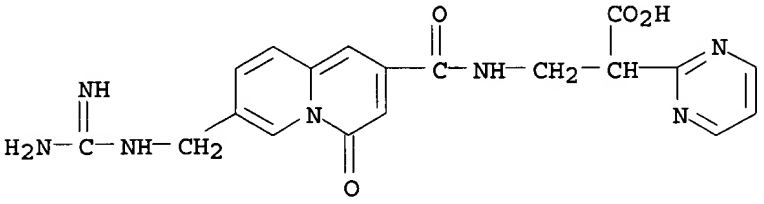
RN 262277-96-3 CAPLUS

~~09/400,992~~

CN 2-Pyrimidineacetic acid, .alpha.-[[[[7-[[(aminoiminomethyl)amino]methyl]-4-oxo-4H-quinolizin-2-yl]carbonyl]amino]methyl]-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

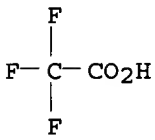
CM 1

CRN 262277-95-2
CMF C19 H19 N7 O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2

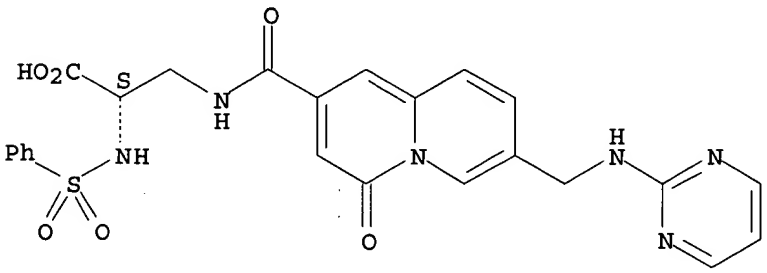


RN 262277-99-6 CAPLUS
CN L-Alanine, 3-[[[4-oxo-7-[(2-pyrimidinylamino)methyl]-4H-quinolizin-2-yl]carbonyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 262277-98-5
CMF C24 H22 N6 O6 S

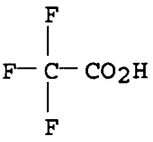
Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

~~09/ 400,992~~



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:98336 CAPLUS
DOCUMENT NUMBER: 132:152134
TITLE: Preparation of heterocyclic-substituted amino acid derivatives as **integrin** receptor antagonists
INVENTOR(S): Duggan, Mark E.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006169	A1	20000210	WO 1999-US16830	19990726
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338275	AA	20000210	CA 1999-2338275	19990726
AU 9951286	A1	20000221	AU 1999-51286	19990726
AU 747784	B2	20020523		
EP 1100506	A1	20010523	EP 1999-935910	19990726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, RO				
JP 2002521450	T2	20020716	JP 2000-562023	19990726
US 6040311	A	20000321	US 1999-362528	19990728

PRIORITY APPLN. INFO.: US 1998-94478P P 19980729
WO 1999-US16830 W 19990726
OTHER SOURCE(S): MARPAT 132:152134

AB Compds. W-X-Y-Z-CR5R6CR7R8CO2R9 [W is a 5- or 6-membered monocyclic arom. or nonarom. ring system or a 9- to 14-membered polycyclic ring system, where one or more of the rings is arom. and each ring system has 1, 2, 3, or 4 heteroatoms (N, O, S) and is optionally substituted; X = (un)substituted (CH2)v or (CH2)vNH(CH2)v (v = 0-6); Y = (un)substituted biaryl ring system comprising 5- or 6-membered arom. rings contg. 0-6 heteroaroms.; Z = CONH, NHCO, CH2CH2, or CH:CH which may be optionally substituted; R5-R9 = H or alkyl, aryl and other substituents] were prepd. as **integrin** receptor antagonists. Thus, 3'-[N-(3,4,5,6-tetrahydropyrimidin-2-yl)amino]biphenyl-4-carbonyl-2(S)-phenylsulfonylamino-.beta.-alanine was prepd. by a multistep scheme involving reactions of m-nitrobenzeneboronic acid, Me p-bromobenzoate, 2-bromopyrimidine, and 2(S)-phenylsulfonylamino-.beta.-alanine tert-Bu ester hydrochloride.

IT **257876-88-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)

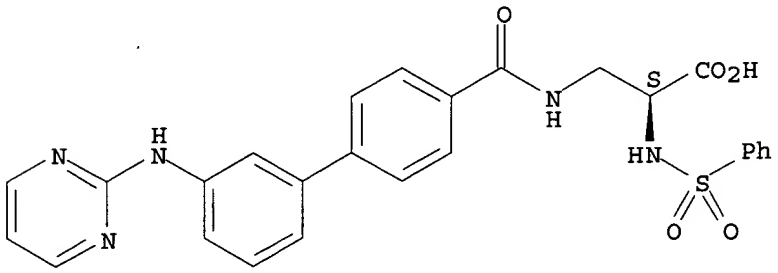
~~09/400,992~~

(prepn. of heterocyclic-substituted amino acid derivs. as **integrin** receptor antagonists)

RN 257876-88-3 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[[3'-(2-pyrimidinylamino)[1,1'-biphenyl]-4-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:94016 CAPLUS

DOCUMENT NUMBER: 132:245846

TITLE: RGD mimetics containing a central hydantoin scaffold: .alpha.v.beta.3 vs .alpha.IIb.beta.3 selectivity requirements

AUTHOR(S): Peyman, Anusch; Wehner, Volkmar; Knolle, Jochen; Stilz, Hans Ulrich; Breipohl, Gerhard; Scheunemann, Karl-Heinz; Carniato, Denis; Ruxer, Jean-Marie; Gourvest, Jean-Francois; Gadek, Thomas R.; Bodary, Sarah

CORPORATE SOURCE: Hoechst Marion Roussel Deutschland GmbH, Frankfurt, D-65926, Germany

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(2), 179-182
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis of a series of RGD mimetic .alpha.v.beta.3 antagonists contg. a hydantoin scaffold is shown. The results demonstrate some of the structural requirements for the design of selective .alpha.v.beta.3 antagonists (vs. .alpha.IIb.beta.3) in terms of the Arg-mimetic, the distance between N- and C-terminus and the lipophilic side chain.

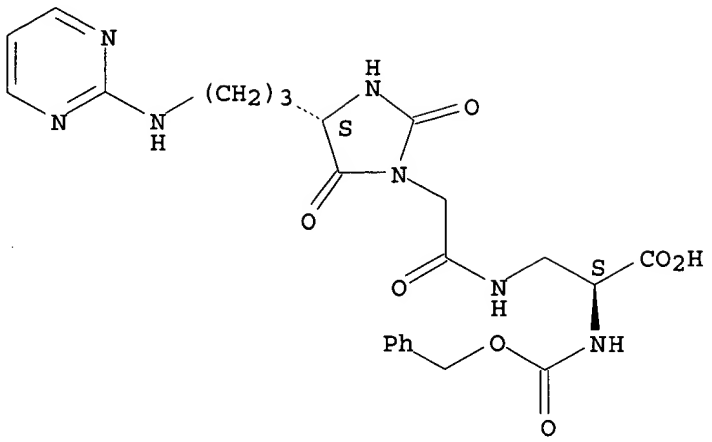
IT **197357-69-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation)
(RGD mimetics contg. a central hydantoin scaffold in relation to .alpha.v.beta.3 vs. .alpha.IIb.beta.3 selectivity requirements)

RN 197357-69-0 CAPLUS

CN L-Alanine, 3-[[[(4S)-2,5-dioxo-4-[3-(2-pyrimidinylamino)propyl]-1-imidazolidinyl]acetyl]amino]-N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

~~09/400,992~~



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

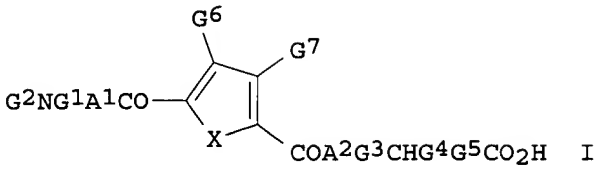
L7 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:15198 CAPLUS
DOCUMENT NUMBER: 132:78464
TITLE: Preparation of thiophene-2,5-dicarboxamides and furan-2,5-dicarboxamides useful in the treatment of cancer
INVENTOR(S): Labrecque, Denis; Lamothe, Serge; Courchesne, Marc; Chan, Laval; Attardo, Giorgio; Meerovitch, Karen
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000486	A1	20000106	WO 1999-IB1221	19990629
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9943853	A1	20000117	AU 1999-43853	19990629
EP 1091952	A1	20010418	EP 1999-926680	19990629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002137947	A1	20020926	US 2002-46396	20020116

PRIORITY APPLN. INFO.: US 1998-91063P P 19980629
WO 1999-IB1221 W 19990629
US 2000-736027 B1 20001221

OTHER SOURCE(S): MARPAT 132:78464
GI

~~09/ 400,992~~



I

AB The title compds. I [X = O, S; A1, A2 = O, S, N; G1, G3, G5 = alkyl chain; G2 = CHA3A4 with A3, A4 = O, N, S, etc.; G4 = aryl, arylsulfonylamino, arylamino; G6, G7 = H, F, Cl, iodo, Br, alkyl], useful in the treatment of cancer, were prepd. E.g., 3-{[5-(3-guanidinopropylcarbamoyl)thiophene-2-carbonyl]amino}-3-phenylpropionic acid was prepd. The IC50 values for fibrinogen binding assay of I were detd. Other properties of I, e.g. inhibition of metastasis in lung cancer model, were also detd.

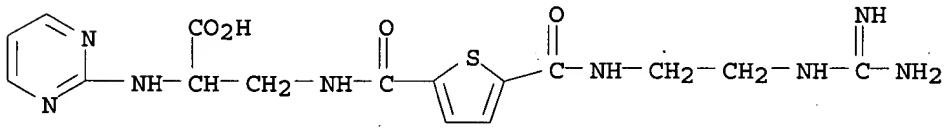
IT **253681-88-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of thiophenedicarboxamides and furandicarboxamides useful in the treatment of cancer)

RN 253681-88-8 CAPLUS

CN Alanine, 3-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-2-thienyl]carbonyl]amino]-N-2-pyrimidinyl-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

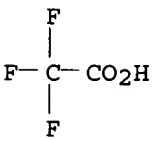
CM 1

CRN 253681-87-7
CMF C16 H20 N8 O4 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:672767 CAPLUS
DOCUMENT NUMBER: 131:299288
TITLE: Acylresorcinol derivatives as selective vitronectin receptor inhibitors

~~09/400,993~~

INVENTOR(S): Kees, Kenneth Lewis; Garrick, Lloyd Michael; Gopalsamy, Ariamala
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952879	A1	19991021	WO 1999-US8180	19990414
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9935610	A1	19991101	AU 1999-35610	19990414
PRIORITY APPLN. INFO.:			US 1998-59579	19980414
			WO 1999-US8180	19990414

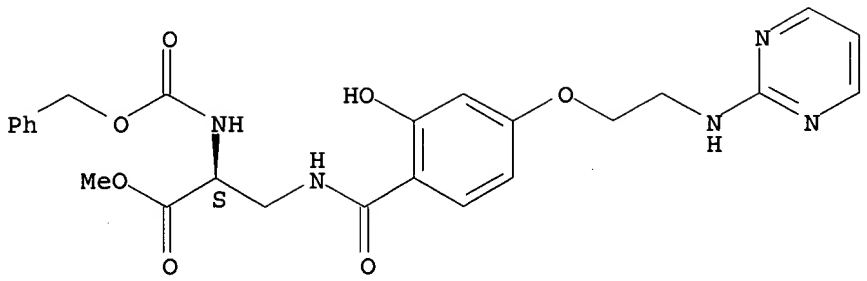
OTHER SOURCE(S): MARPAT 131:299288
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. of formula I are useful in the treatment of various disorders including, but not limited to, cancer, angiogenesis, restenosis, inflammation, bone diseases, and as antiviral agents [wherein G = amidino and cyclic analogs, 2-pyridinyl, 2-pyrimidinyl, other similar N-contg. groups; R1, R2 = H, alkyl, aralkyl, heterocycloalkylalkyl; R3 = H, aryl, heterocycloalkyl; R4 = H, OH or NH2 or derivs.; provided that both R3 and R4 cannot be H; R5 = H, alkyl, optionally substituted with a terminal prodrug group; n = 1-4; and pharmaceutically acceptable salts]. Novel methods of making I are also provided. The compds. are selective inhibitors of certain **integrin** receptors such as .alpha.v.beta.3. Over 300 synthetic examples are given. For instance, the title compd. II.HCl was prepd. in 4 steps from the acid III, specifically: (1) amidation with 2S-(benzenesulfonylamino)-.beta.-alanine Et ester; (2) sapon. of the Et ester; (3) partial hydrogenation of the pyrimidine nucleus; and (4) acidic reesterification. II.HCl had an IC50 value of 0.12 .mu.M in an osteopontin-.alpha.v.beta.3 cell attachment assay, and 0.15 .mu.M in an osteoclast bone pitting assay.

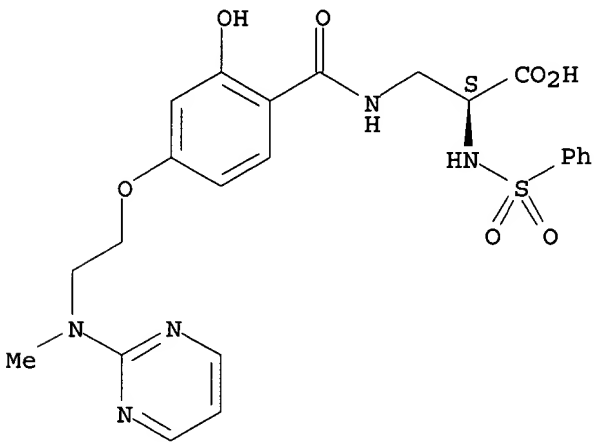
IT **247128-00-3P 247128-01-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of acylresorcinol derivs. as selective vitronectin receptor inhibitors)
RN 247128-00-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247128-01-4 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(methyl-2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

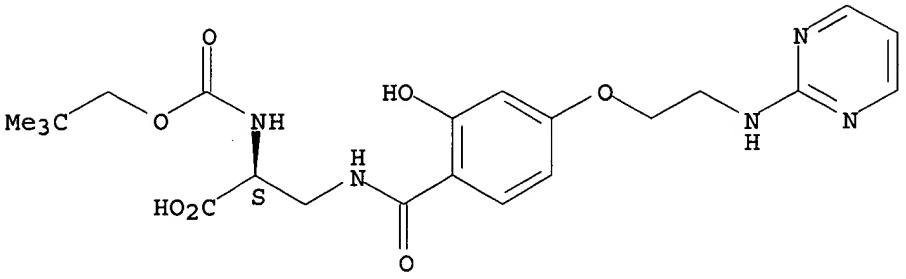


IT **247124-79-4P 247124-80-7P 247124-81-8P**
247124-82-9P 247124-83-0P 247124-84-1P
247124-85-2P 247124-86-3P 247124-87-4P
247124-88-5P 247124-89-6P 247124-90-9P
247124-91-0P 247124-92-1P 247124-93-2P
247124-94-3P 247124-95-4P 247124-96-5P
247124-97-6P 247124-98-7P 247124-99-8P
247125-00-4P 247125-01-5P 247125-02-6P
247125-03-7P 247125-04-8P 247125-05-9P
247125-06-0P 247125-07-1P 247125-08-2P
247125-09-3P 247125-10-6P 247125-11-7P
247125-12-8P 247125-13-9P 247125-14-0P
247125-15-1P 247125-16-2P 247125-17-3P
247125-18-4P 247125-19-5P 247125-20-8P
247127-05-5P 247127-06-6P 247127-13-5P
247127-18-0P 247127-19-1P 247127-20-4P
247127-21-5P 247127-23-7P 247127-34-0P
247127-35-1P 247127-36-2P 247127-39-5P
247127-74-8P 247127-79-3P 247127-83-9P
247127-84-0P 247127-87-3P 247127-94-2P
247127-98-6P 247128-00-3P 247128-01-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(target compd.; prepn. of acylresorcinol derivs. as selective vitronectin receptor inhibitors)

~~09/400,992~~

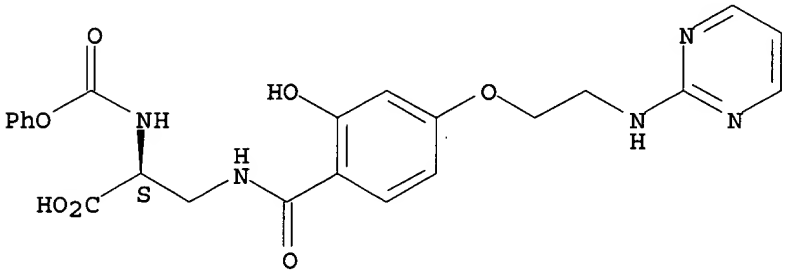
RN 247124-79-4 CAPLUS
CN L-Alanine, N-[(2,2-dimethylpropoxy)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



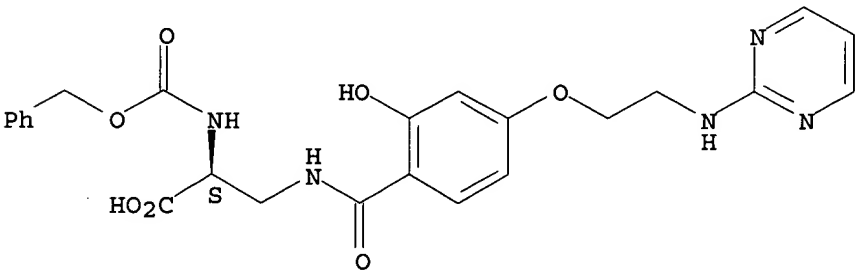
RN 247124-80-7 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(phenoxycarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



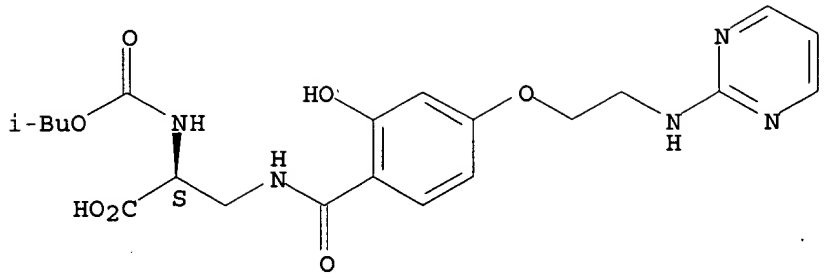
RN 247124-81-8 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



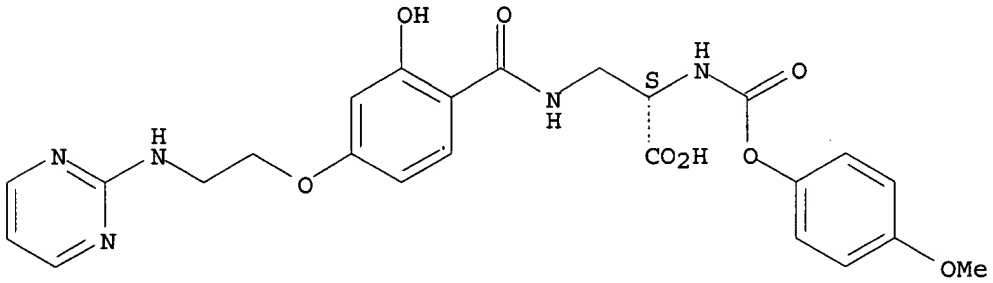
RN 247124-82-9 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(2-methylpropoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



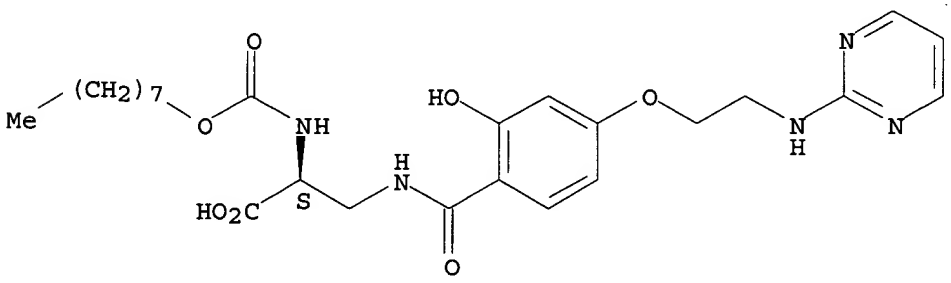
RN 247124-83-0 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(4-methoxyphenoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247124-84-1 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(octyloxy)carbonyl]- (9CI) (CA INDEX NAME)

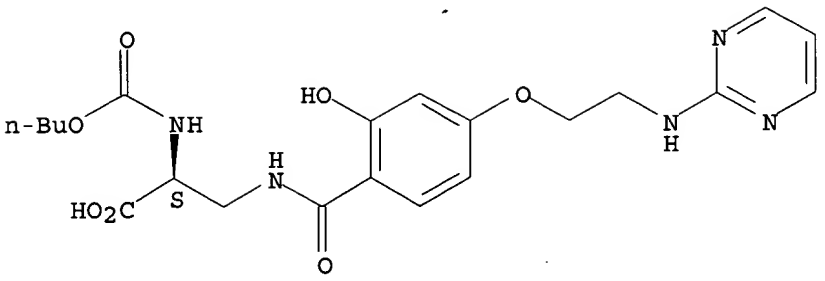
Absolute stereochemistry.



RN 247124-85-2 CAPLUS
CN L-Alanine, N-(butoxycarbonyl)-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

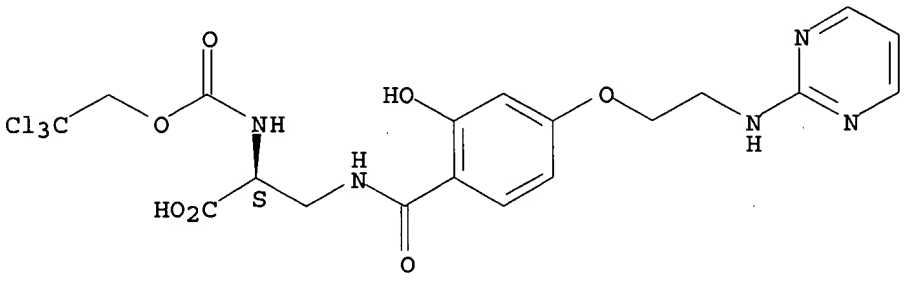
Absolute stereochemistry.

~~09/400,992~~



RN 247124-86-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(2,2,2-trichloroethoxy)carbonyl]- (9CI) (CA INDEX NAME)

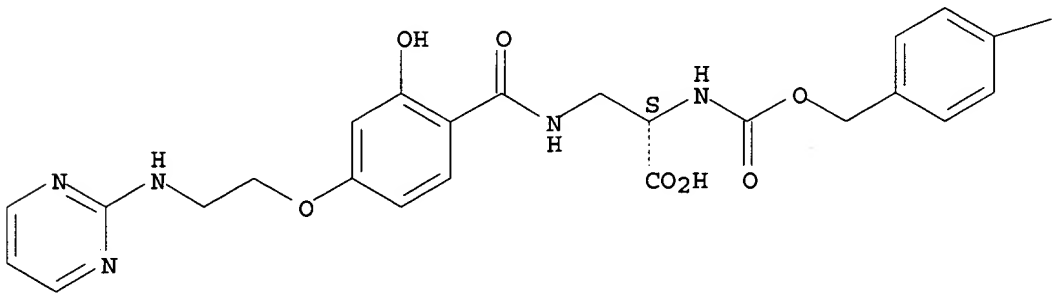
Absolute stereochemistry.



RN 247124-87-4 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(4-nitrophenyl)methoxy]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

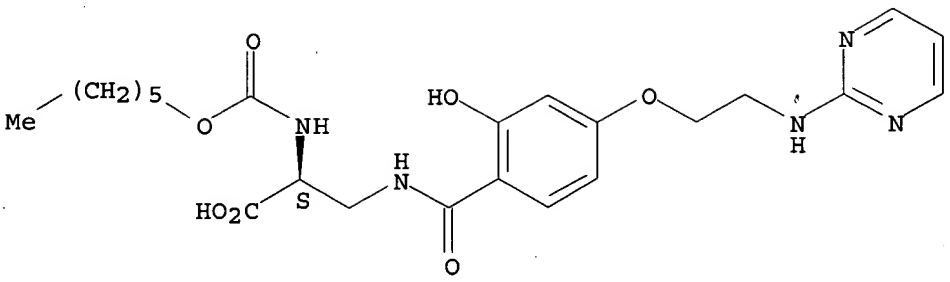


PAGE 1-B

RN 247124-88-5 CAPLUS
CN L-Alanine, N-[(hexyloxy)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

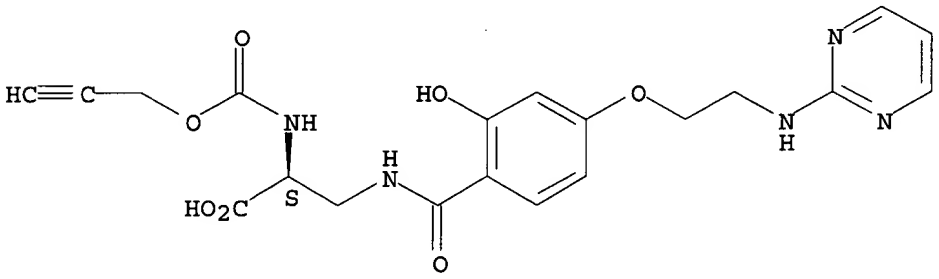
Absolute stereochemistry.

~~09/400,992~~



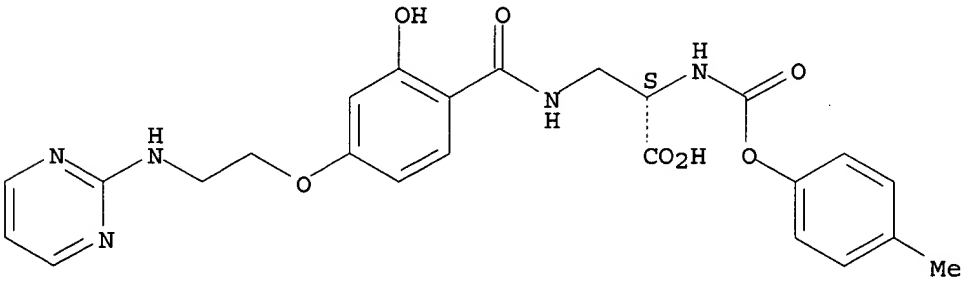
RN 247124-89-6 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(2-propynyloxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



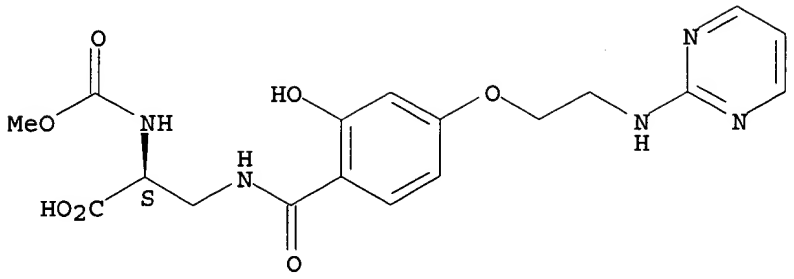
RN 247124-90-9 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(4-methylphenoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



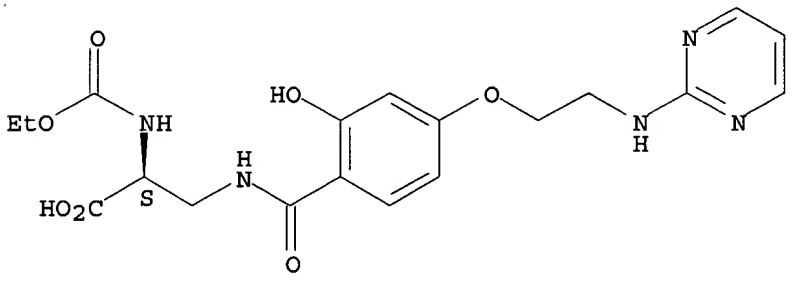
RN 247124-91-0 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(methoxycarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



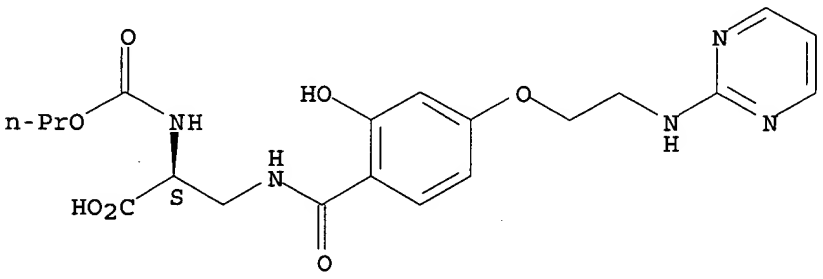
RN 247124-92-1 CAPLUS
CN L-Alanine, N-(ethoxycarbonyl)-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247124-93-2 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(propoxycarbonyl)- (9CI) (CA INDEX NAME)

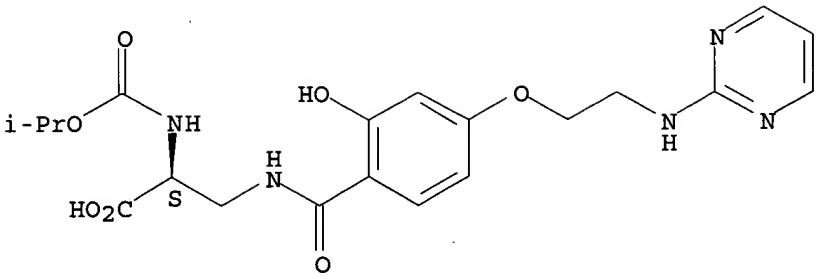
Absolute stereochemistry.



RN 247124-94-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(1-methylethoxy)carbonyl]- (9CI) (CA INDEX NAME)

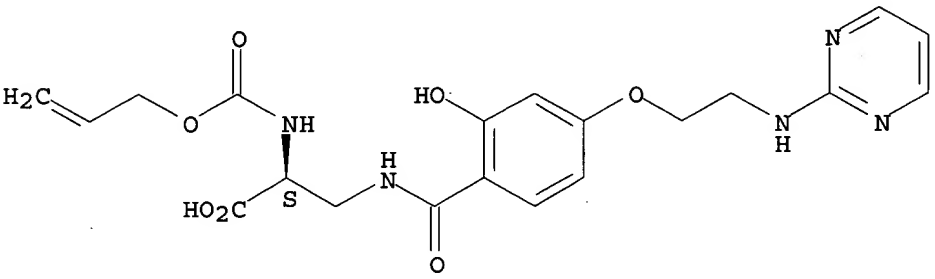
Absolute stereochemistry.

~~88/ 400, 992~~



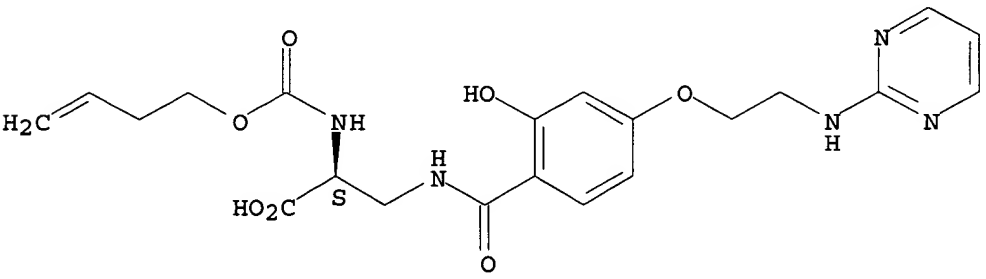
RN 247124-95-4 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(2-propenyloxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247124-96-5 CAPLUS
CN L-Alanine, N-[(3-butenyloxy)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

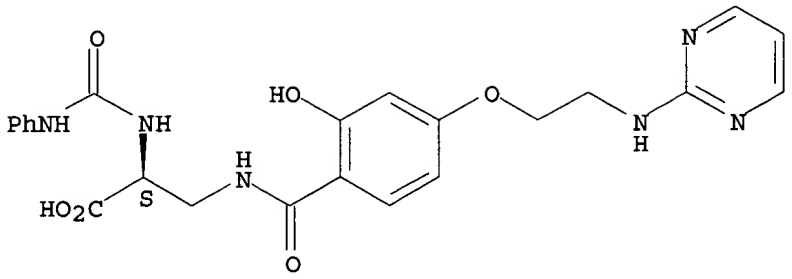
Absolute stereochemistry.



RN 247124-97-6 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(phenylamino)carbonyl]- (9CI) (CA INDEX NAME)

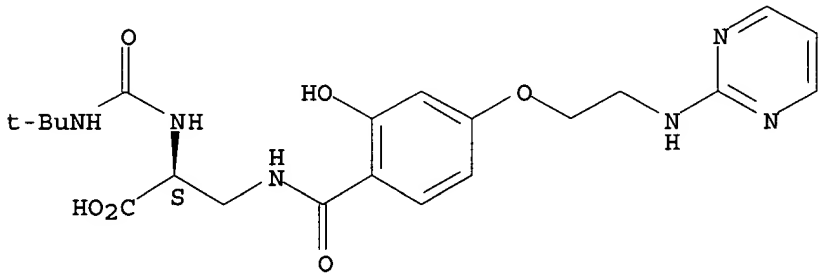
Absolute stereochemistry.

~~09/400,992~~



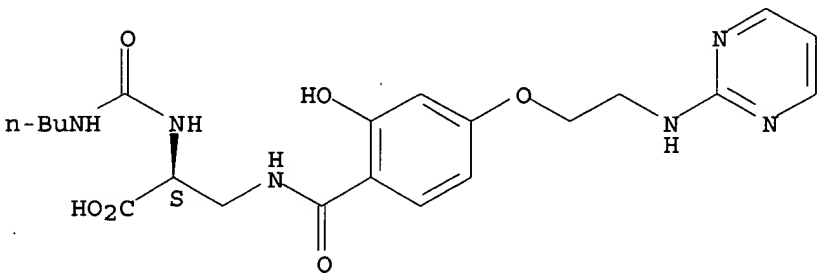
RN 247124-98-7 CAPLUS
CN L-Alanine, N-[[(1,1-dimethylethyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247124-99-8 CAPLUS
CN L-Alanine, N-[(butylamino)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

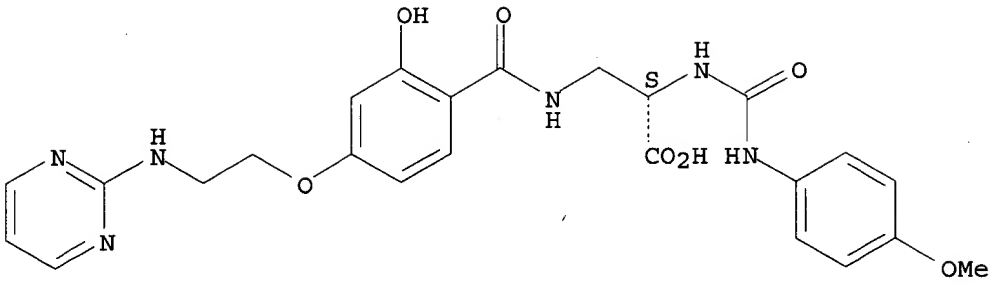
Absolute stereochemistry.



RN 247125-00-4 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(4-methoxyphenyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

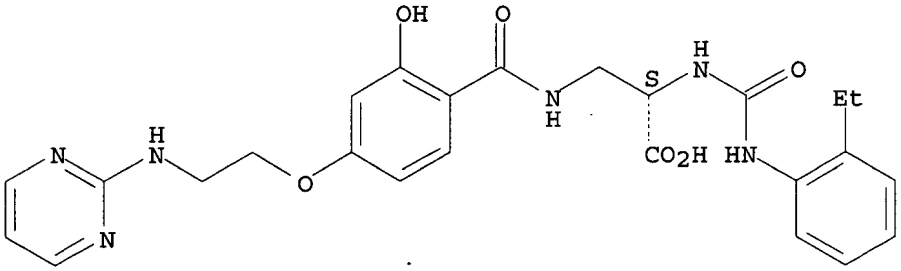
Absolute stereochemistry.

~~09/ 400,998~~



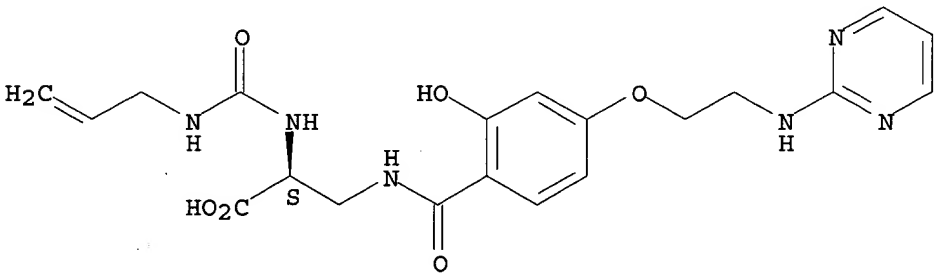
RN 247125-01-5 CAPLUS
CN L-Alanine, N-[[(2-ethylphenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



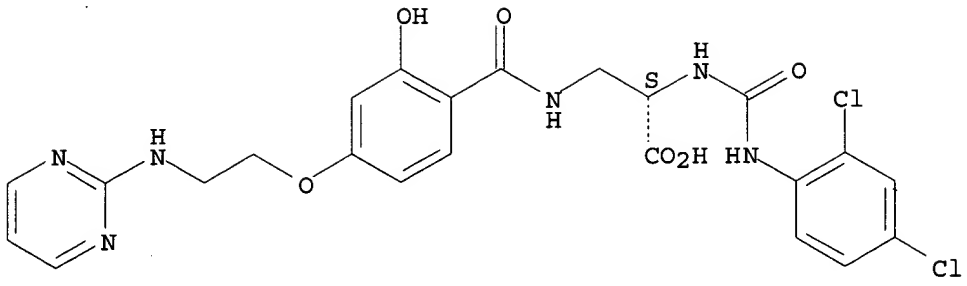
RN 247125-02-6 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(2-propenylamino)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



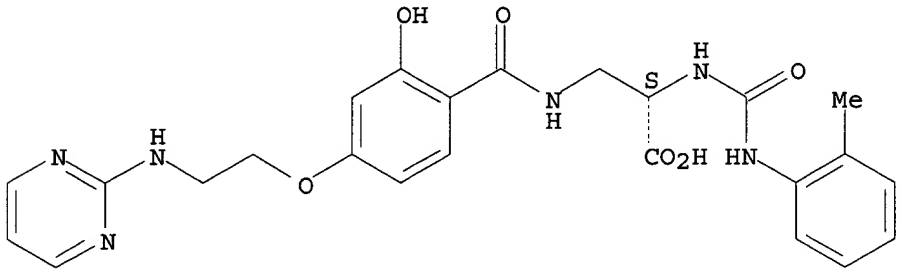
RN 247125-03-7 CAPLUS
CN L-Alanine, N-[[(2,4-dichlorophenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



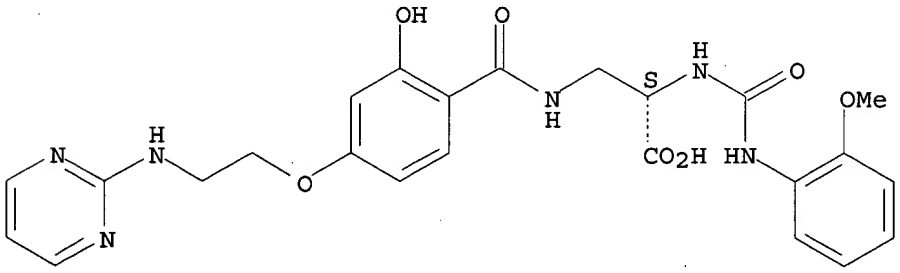
RN 247125-04-8 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(2-methylphenyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247125-05-9 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(2-methoxyphenyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

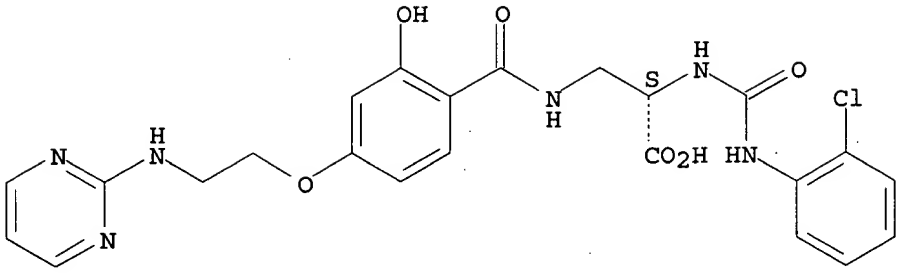
Absolute stereochemistry.



RN 247125-06-0 CAPLUS
CN L-Alanine, N-[[(2-chlorophenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

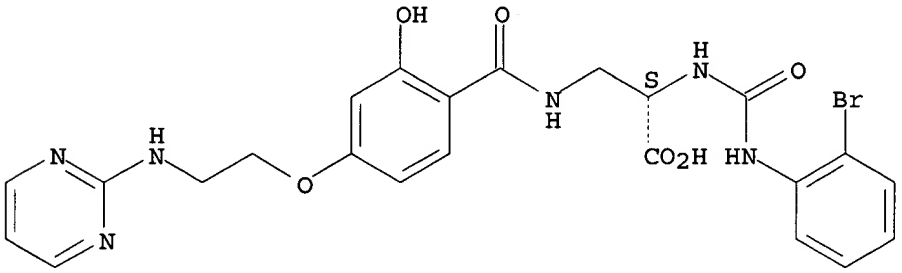
Absolute stereochemistry.

~~09/400,992~~



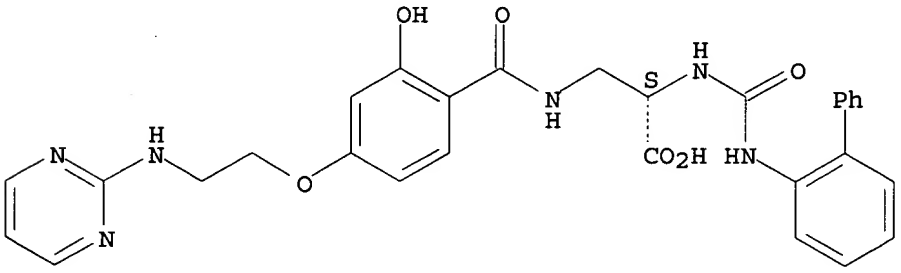
RN 247125-07-1 CAPLUS
CN L-Alanine, N-[[(2-bromophenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247125-08-2 CAPLUS
CN L-Alanine, N-[([1,1'-biphenyl]-2-ylamino)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

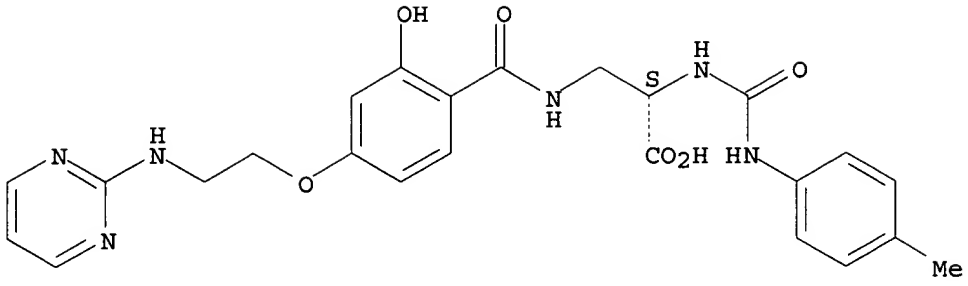
Absolute stereochemistry.



RN 247125-09-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(4-methylphenyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

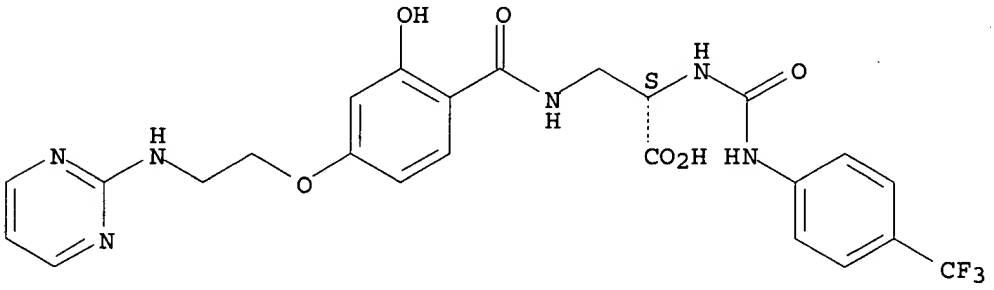
Absolute stereochemistry.

~~09/400,992~~



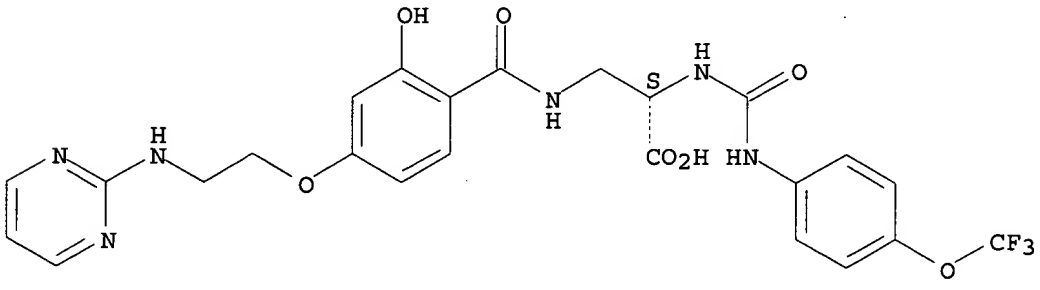
RN 247125-10-6 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[[4-(trifluoromethyl)phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247125-11-7 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

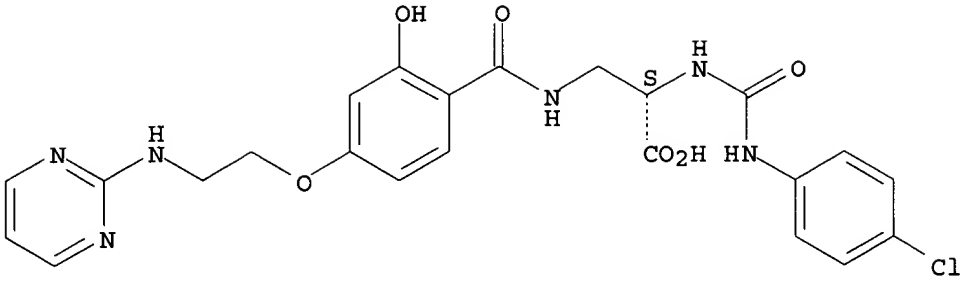
Absolute stereochemistry.



RN 247125-12-8 CAPLUS
CN L-Alanine, N-[[(4-chlorophenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

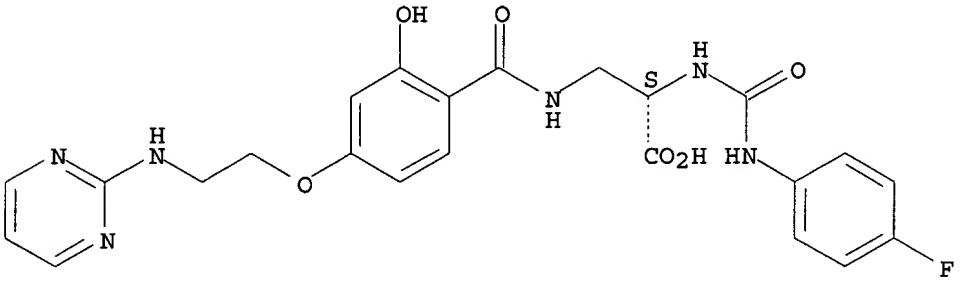
Absolute stereochemistry.

~~09/ 400,992~~



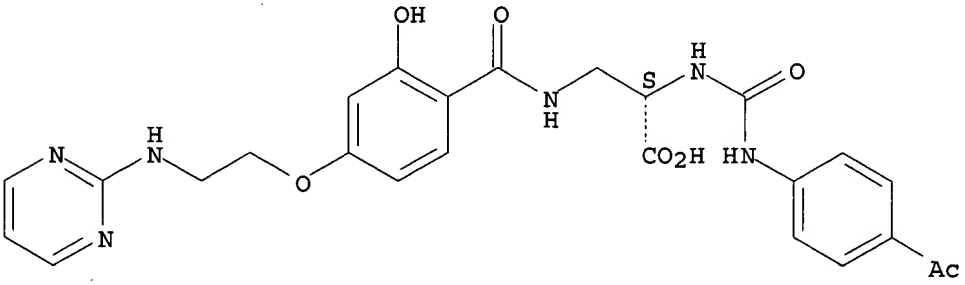
RN 247125-13-9 CAPLUS
CN L-Alanine, N-[[(4-fluorophenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247125-14-0 CAPLUS
CN L-Alanine, N-[[(4-acetylphenyl)amino]carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247125-15-1 CAPLUS
CN Benzoic acid, 4-[[[[(1S)-1-carboxy-2-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]ethyl]amino]carbonyl]amino]-, 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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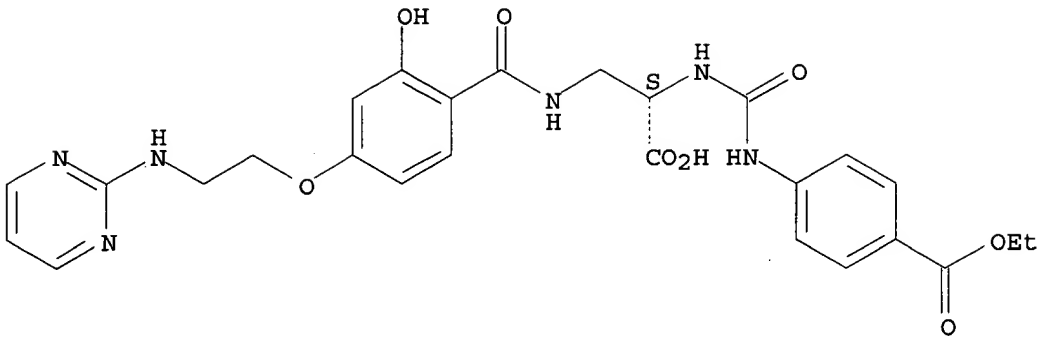
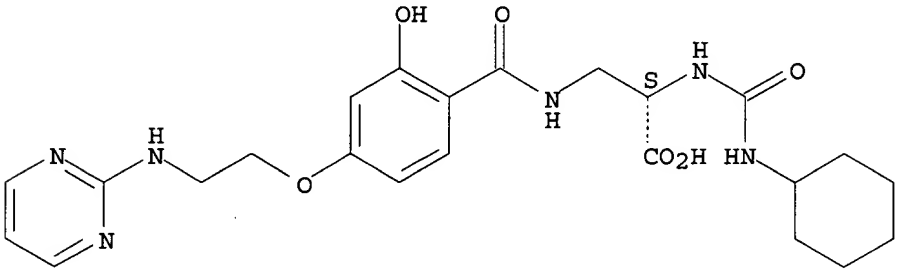


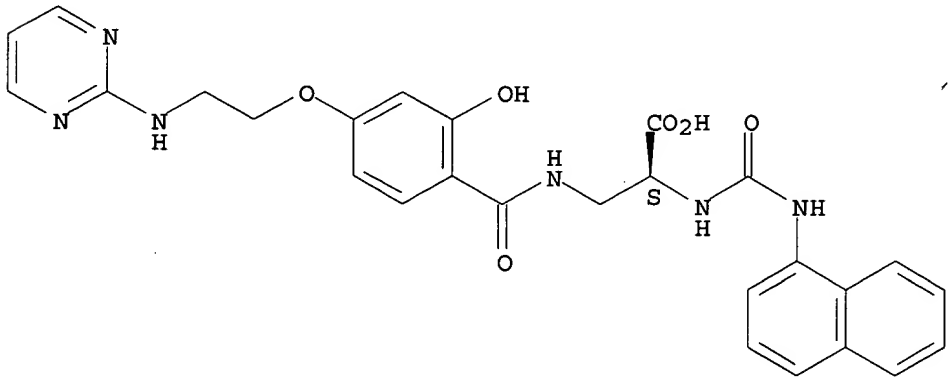
RN 247125-16-2 CAPLUS
CN L-Alanine, N-[(cyclohexylamino)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



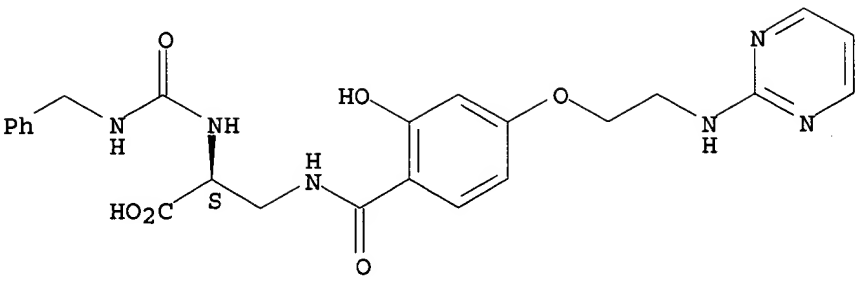
RN 247125-17-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(1-naphthalenylamino)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



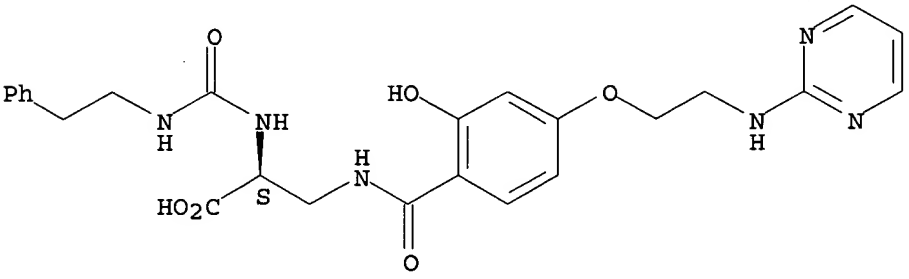
RN 247125-18-4 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(phenylmethyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



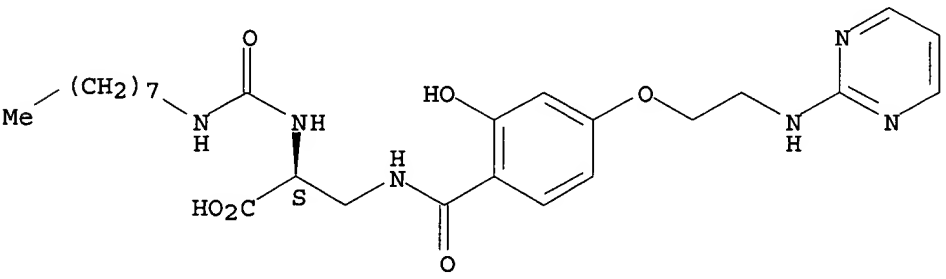
RN 247125-19-5 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[[(2-phenylethyl)amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247125-20-8 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(octylamino)carbonyl]- (9CI) (CA INDEX NAME)

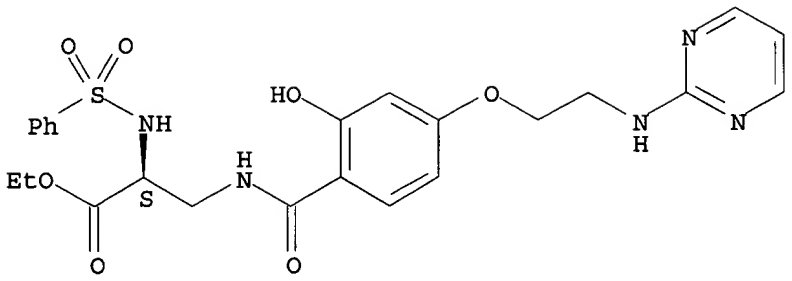
Absolute stereochemistry.



RN 247127-05-5 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(phenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)

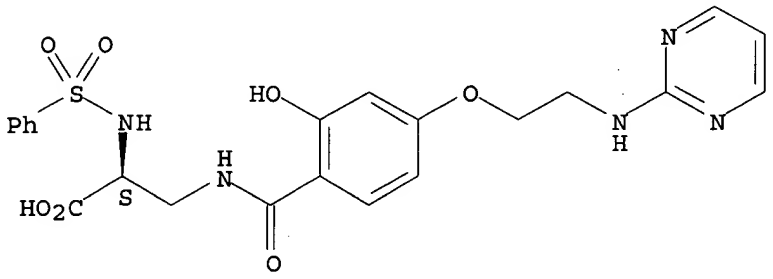
Absolute stereochemistry.

~~09/ 400,992~~

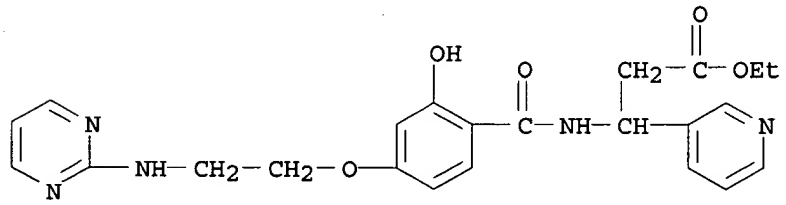


RN 247127-06-6 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

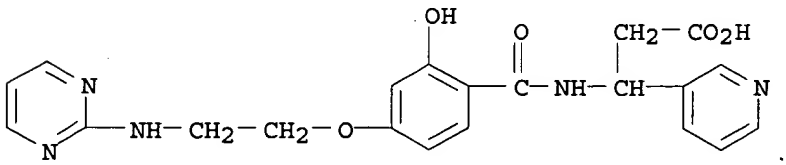
Absolute stereochemistry.



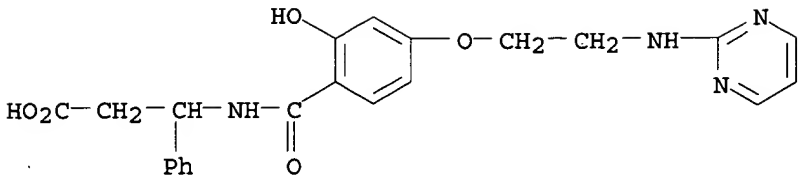
RN 247127-13-5 CAPLUS
CN 3-Pyridinepropanoic acid, .beta.-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



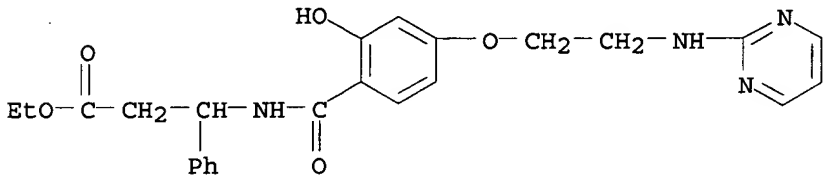
RN 247127-18-0 CAPLUS
CN 3-Pyridinepropanoic acid, .beta.-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)



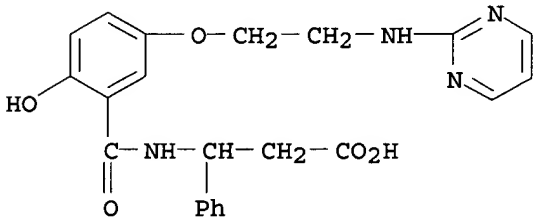
RN 247127-19-1 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)



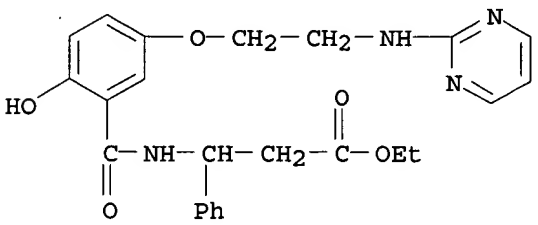
RN 247127-20-4 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



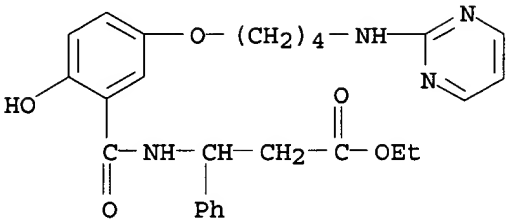
RN 247127-21-5 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-5-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)



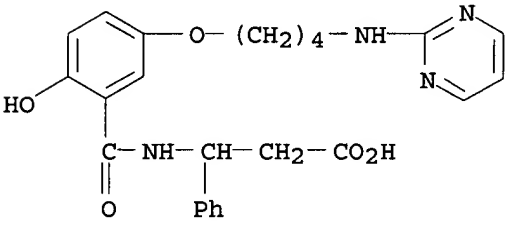
RN 247127-23-7 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-5-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 247127-34-0 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-5-[4-(2-pyrimidinylamino)butoxy]benzoyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

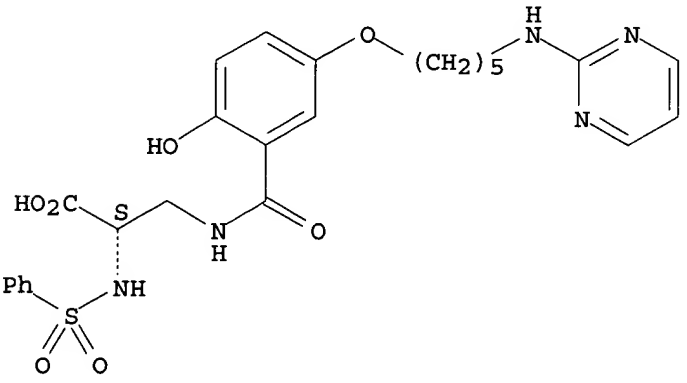


RN 247127-35-1 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-5-[4-(2-pyrimidinylamino)butoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)



RN 247127-36-2 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-5-[[5-(2-pyrimidinylamino)pentyl]oxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247127-39-5 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[4-(2-pyrimidinyl)butoxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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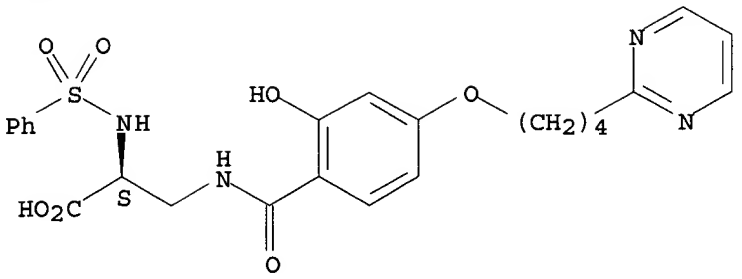
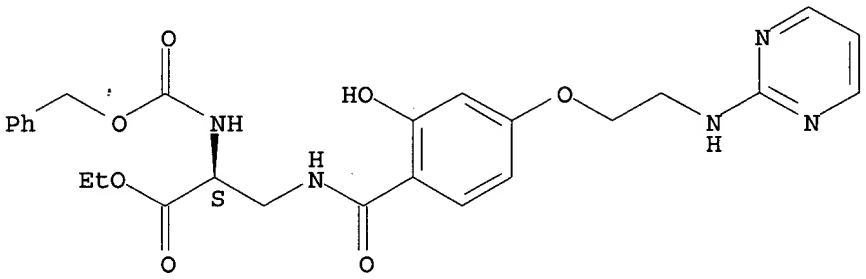


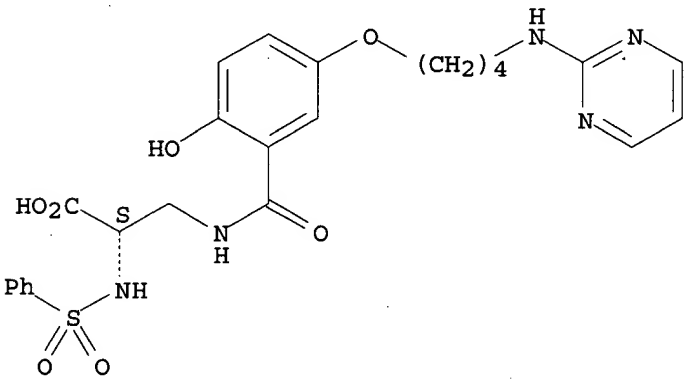
RN 247127-74-8 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



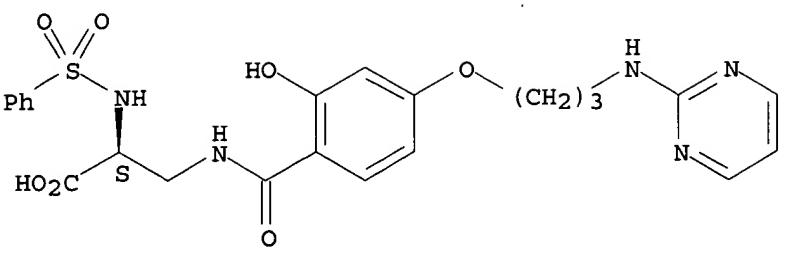
RN 247127-79-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-5-[4-(2-pyrimidinylamino)butoxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

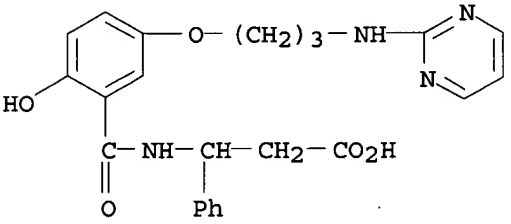


RN 247127-83-9 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[3-(2-pyrimidinylamino)propoxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

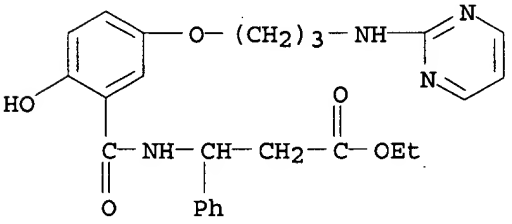
Absolute stereochemistry.



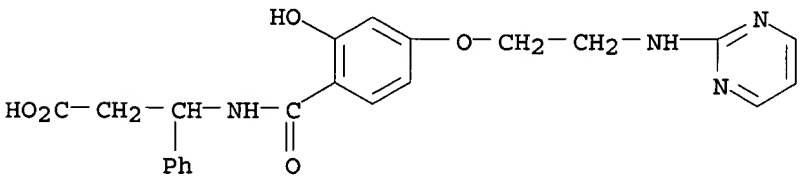
RN 247127-84-0 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-5-[3-(2-pyrimidinylamino)propoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)



RN 247127-87-3 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-5-[3-(2-pyrimidinylamino)propoxy]benzoyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 247127-94-2 CAPLUS
CN Benzenepropanoic acid, .beta.-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)



HCl

RN 247127-98-6 CAPLUS

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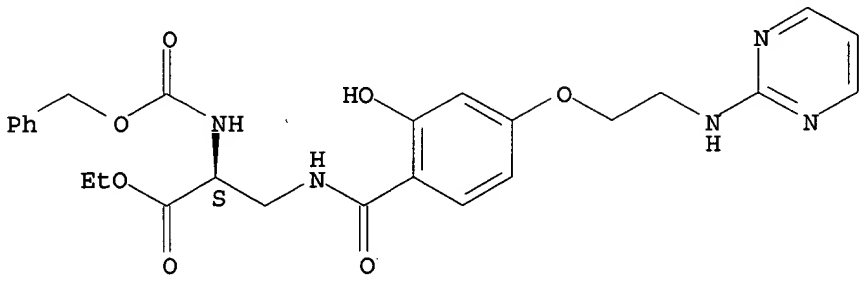
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

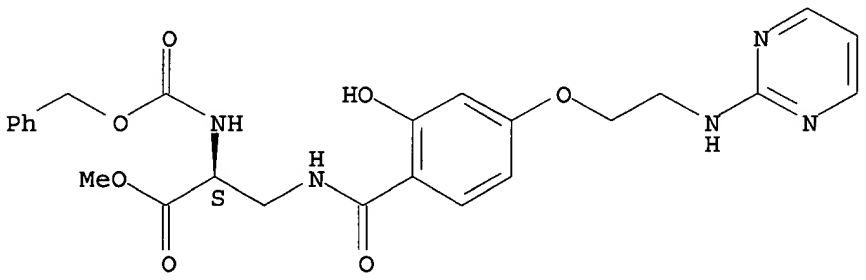
Absolute stereochemistry.



● HCl

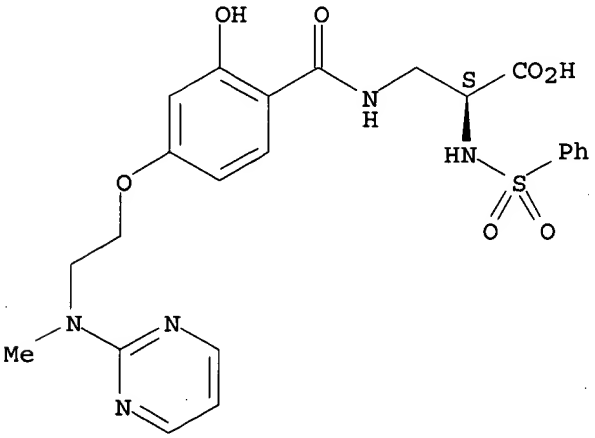
RN 247128-00-3 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247128-01-4 CAPLUS
CN L-Alanine, 3-[[2-hydroxy-4-[2-(methyl-2-pyrimidinylamino)ethoxy]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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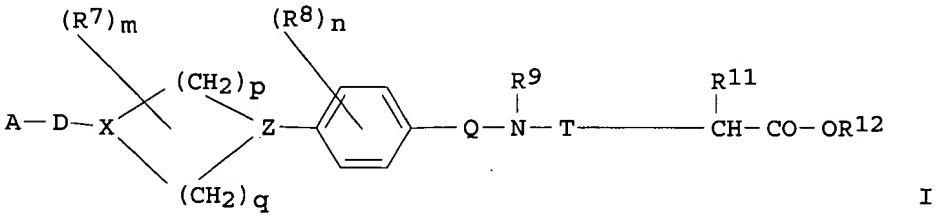
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:672755 CAPLUS
DOCUMENT NUMBER: 131:299455
TITLE: Preparation of aminopiperidine moiety-containing heterocyclic compounds as **integrin** .alpha.v.beta.3 antagonists
INVENTOR(S): Ishikawa, Minoru; Murakami, Shoichi; Yamamoto, Mikio; Kubota, Dai; Hachisu, Mitsugu; Katano, Kiyoaki; Ajito, Keiichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952872	A1	19991021	WO 1999-JP1903	19990409
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2327673	AA	19991021	CA 1999-2327673	19990409
AU 9931678	A1	19991101	AU 1999-31678	19990409
EP 1074543	A1	20010207	EP 1999-913611	19990409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6420558	B1	20020716	US 2000-673017	20001010

PRIORITY APPLN. INFO.: JP 1998-97066 A 19980409
WO 1999-JP1903 W 19990409
OTHER SOURCE(S): MARPAT 131:299455
GI



I

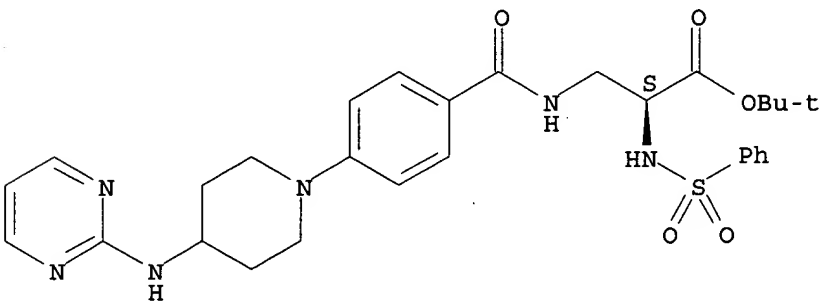
AB The title compds. I [A represents a 5- to 7-membered heterocycle contg. two nitrogen atoms; D represents NH2, CH2, etc.; X and Z represent each CH or N; R7 and R8 represent each alkyl, halogeno, etc.; Q represents CO, CH2, etc.; R9 represents H, alkyl, aralkyl, etc.; T = (CHR10)a; R10 represents H, alkynyl, etc.; R11 represents H, substituted amino, etc.; R12 represents H or alkyl; m is from 0 to 5; n is from 0 to 4; p and q are each from 1 to 3; and a is 0 or 1] are prepd. I have .alpha.v.beta.3

antagonism, cell adhesion inhibitory effect, GP IIb/IIIa antagonism and/or human platelet aggregation inhibitory effect. I are useful in the treatment of cardiovascular diseases, diseases in assocn. with neovascularization, cerebrovascular diseases, etc. In an in vitro test for **integrin** .alpha.v.beta.3 antagonism, 18 compds. of this invention showed IC50 values .ltoreq. 1 nM.

IT **247033-63-2P 247033-64-3P 247033-66-5P**
247033-67-6P 247033-70-1P 247033-73-4P
247033-74-5P 247033-75-6P 247033-76-7P
247033-83-6P 247033-84-7P 247034-06-6P
247034-07-7P 247034-09-9P 247034-10-2P
247034-14-6P 247034-16-8P 247034-24-8P
247034-26-0P 247034-30-6P 247034-33-9P
247034-37-3P 247034-38-4P 247034-50-0P
247034-51-1P 247034-52-2P 247034-53-3P
247034-55-5P 247034-56-6P 247034-57-7P
247034-61-3P 247034-62-4P 247034-63-5P
247034-64-6P 247034-66-8P 247034-67-9P
247034-71-5P 247034-72-6P 247034-74-8P
247034-76-0P 247034-77-1P 247034-78-2P
247034-79-3P 247034-81-7P 247034-82-8P
247034-84-0P 247034-85-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of aminopiperidine moiety-contg. heterocyclic compds. as **integrin** .alpha.v.beta.3 antagonists)

RN 247033-63-2 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

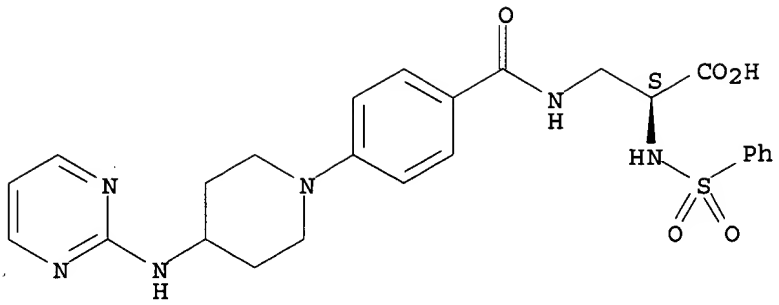
Absolute stereochemistry. Rotation (+).



RN 247033-64-3 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

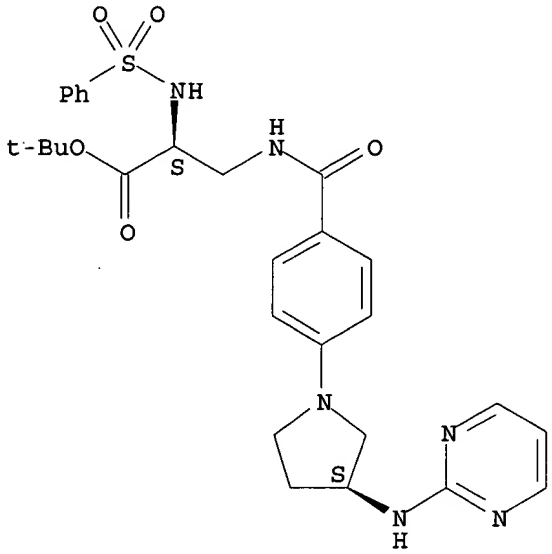
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



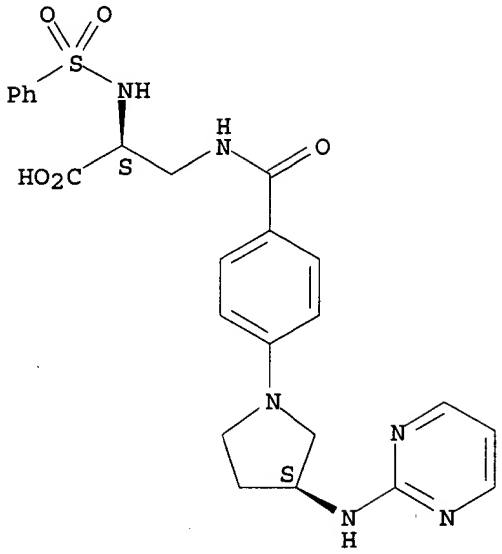
RN 247033-66-5 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-pyrrolidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



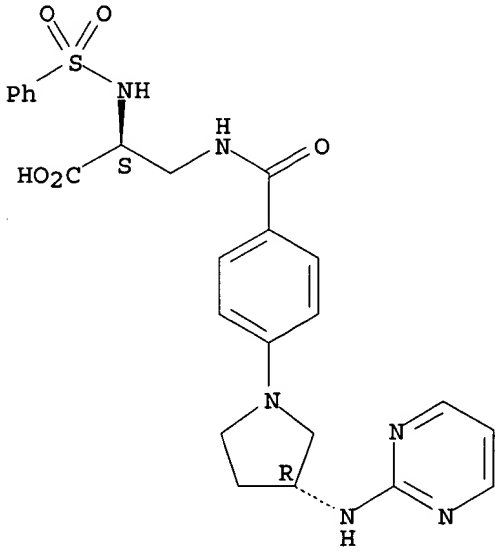
RN 247033-67-6 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3S)-3-(2-pyrimidinylamino)-1-pyrrolidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



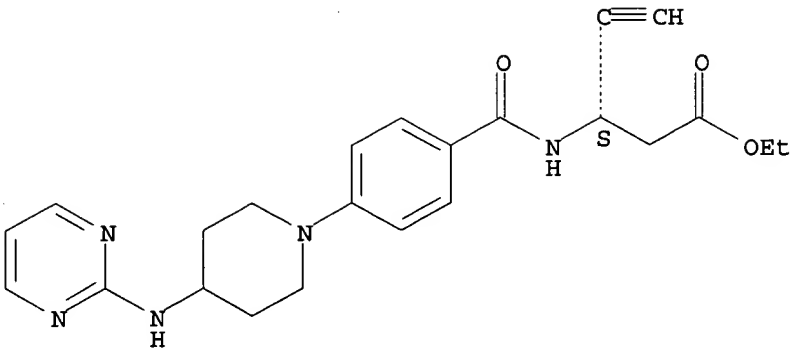
RN 247033-70-1 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[(3R)-3-(2-pyrimidinylamino)-1-pyrrolidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



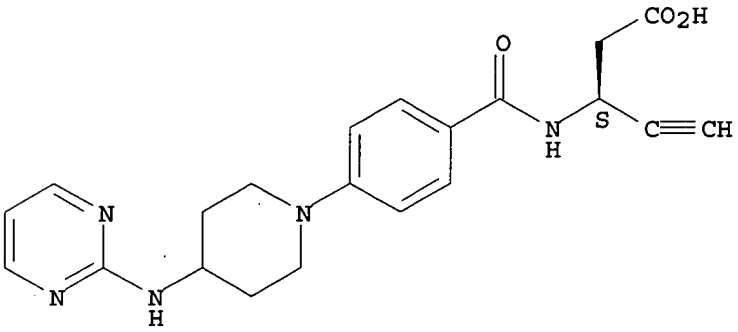
RN 247033-73-4 CAPLUS
CN 4-Pentynoic acid, 3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, ethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



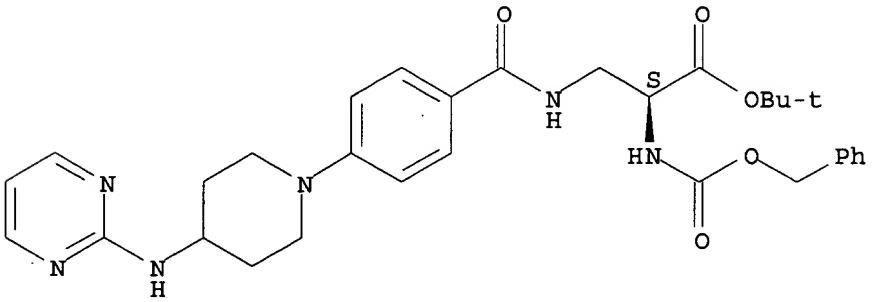
RN 247033-74-5 CAPLUS
CN 4-Pentynoic acid, 3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



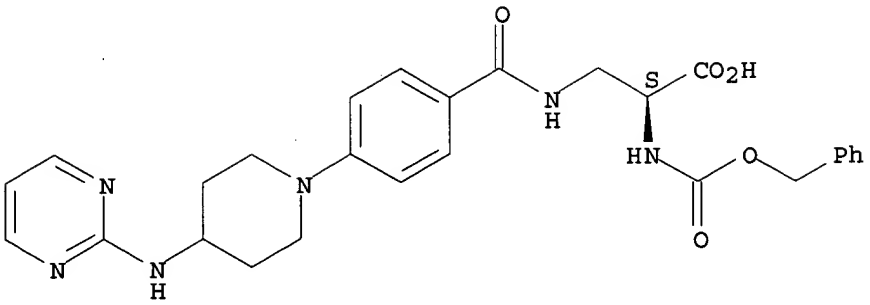
RN 247033-75-6 CAPLUS
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



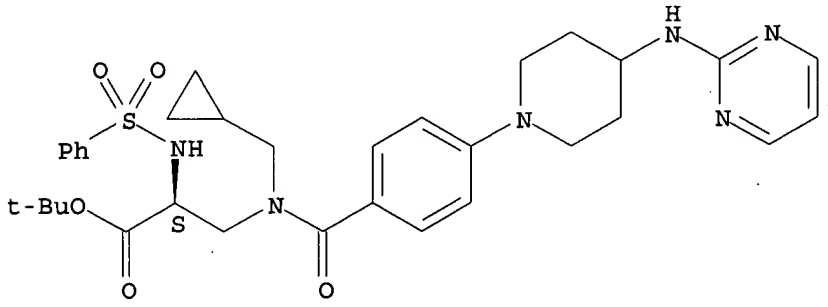
RN 247033-76-7 CAPLUS
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



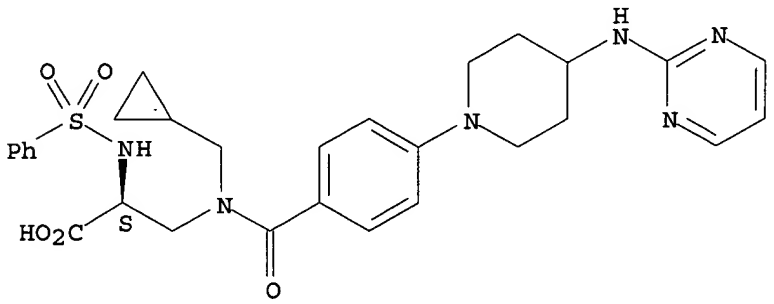
RN 247033-83-6 CAPLUS
CN L-Alanine, 3-[(cyclopropylmethyl)[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



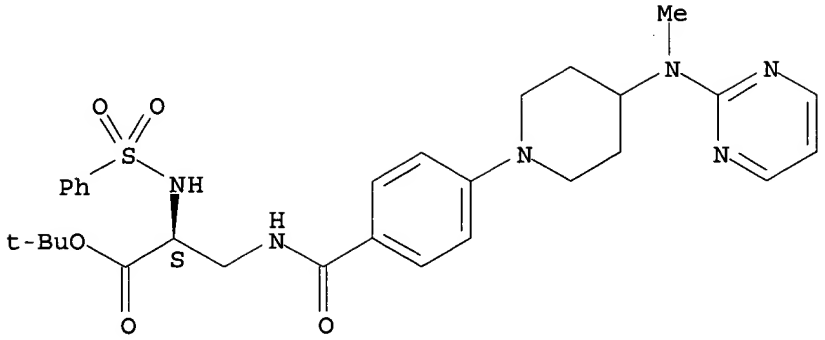
RN 247033-84-7 CAPLUS
CN L-Alanine, 3-[(cyclopropylmethyl)[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



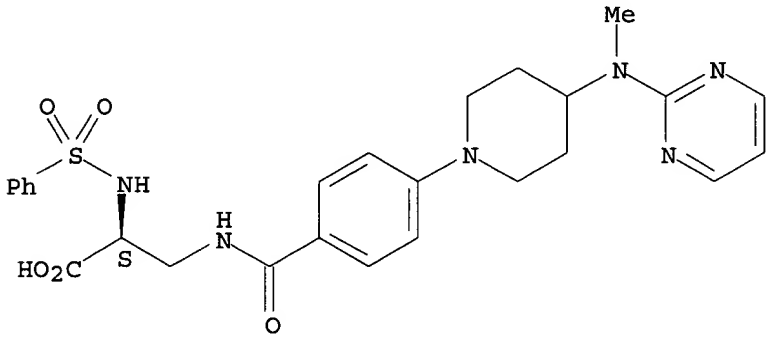
RN 247034-06-6 CAPLUS
CN L-Alanine, 3-[[4-[4-(methyl-2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



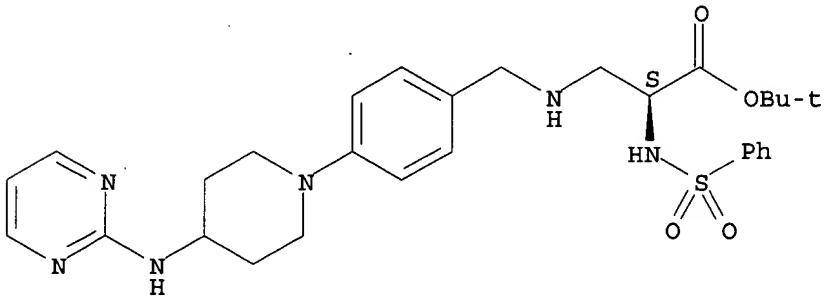
RN 247034-07-7 CAPLUS
CN L-Alanine, 3-[[4-[4-(methyl-2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247034-09-9 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]phenyl]methyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

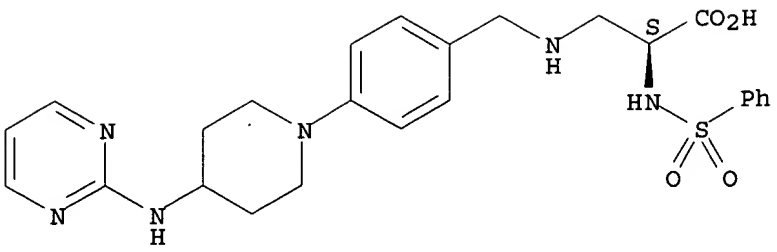
Absolute stereochemistry. Rotation (+).



RN 247034-10-2 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]phenyl]methyl]amino]- (9CI) (CA INDEX NAME)

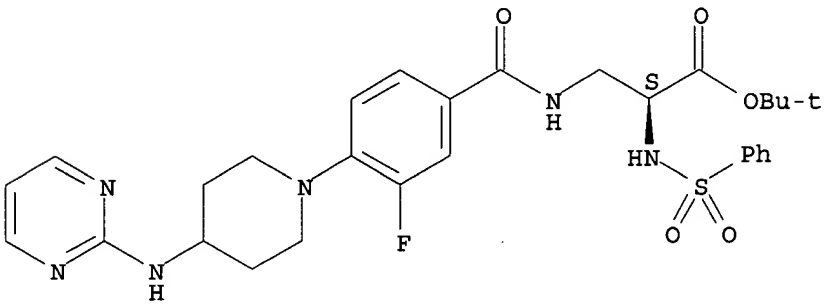
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



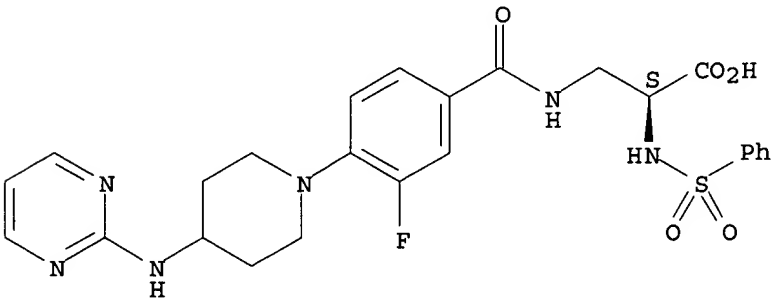
RN 247034-14-6 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 247034-16-8 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

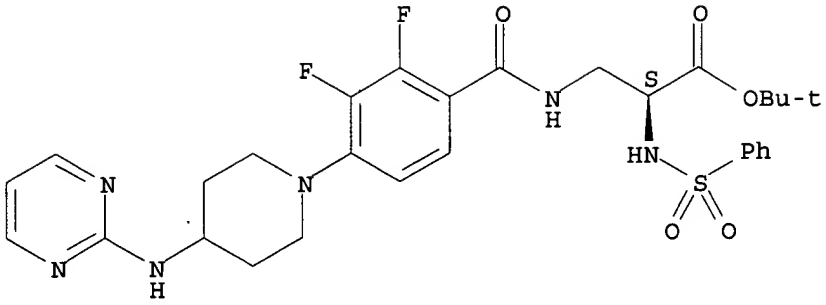
Absolute stereochemistry. Rotation (+).



RN 247034-24-8 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

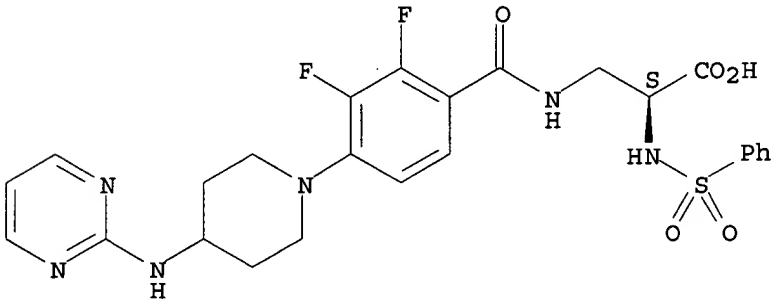
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



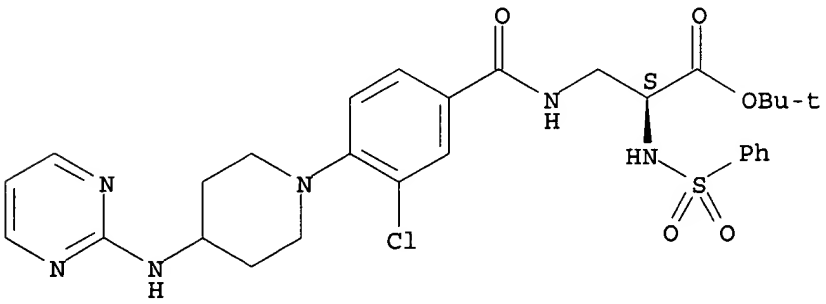
RN 247034-26-0 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 247034-30-6 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

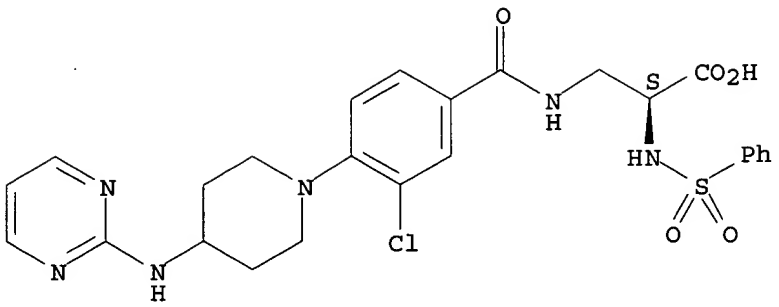
Absolute stereochemistry. Rotation (+).



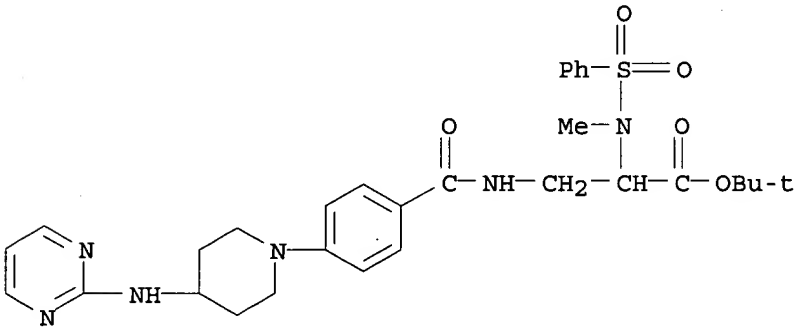
RN 247034-33-9 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

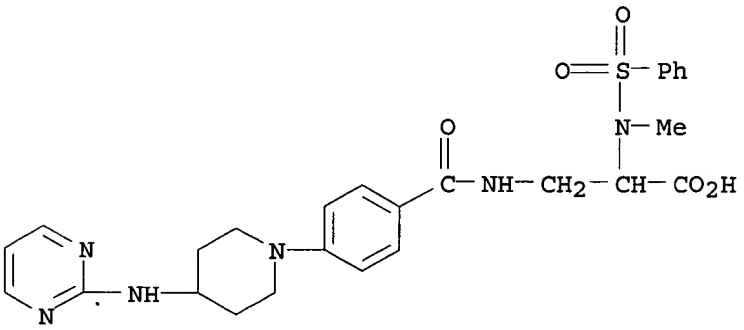
~~09/400,992~~



RN 247034-37-3 CAPLUS
CN Alanine, N-methyl-N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



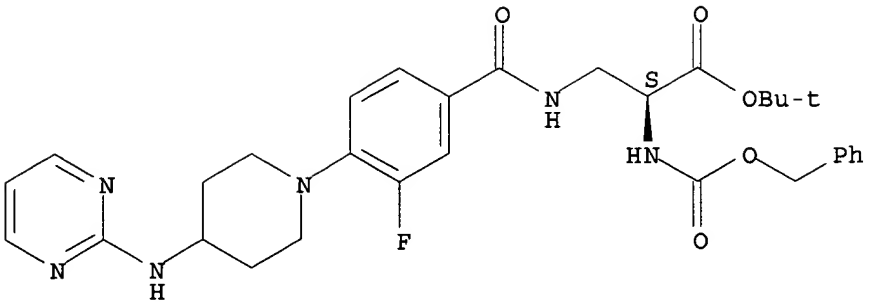
RN 247034-38-4 CAPLUS
CN Alanine, N-methyl-N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)



RN 247034-50-0 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

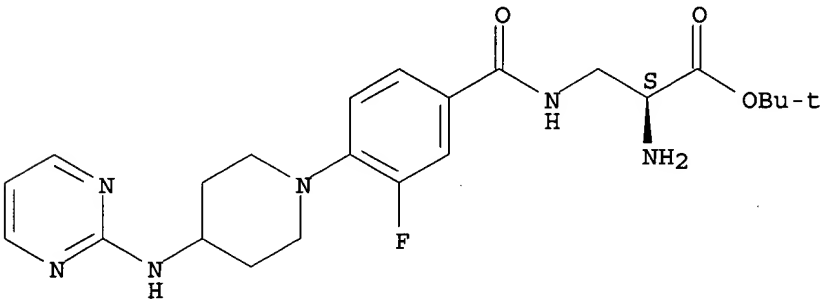
Absolute stereochemistry. Rotation (-).

~~09/400,992~~



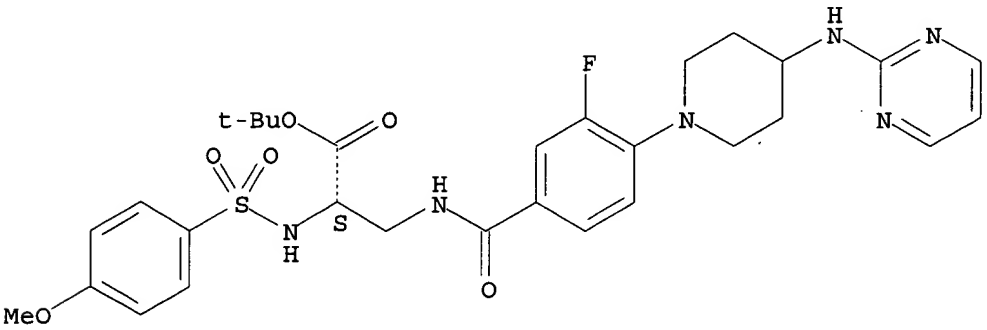
RN 247034-51-1 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 247034-52-2 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-methoxyphenyl)sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

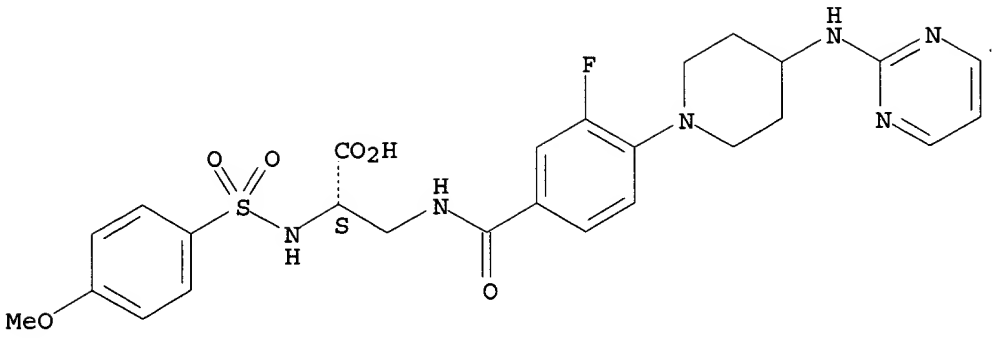
Absolute stereochemistry. Rotation (+).



RN 247034-53-3 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

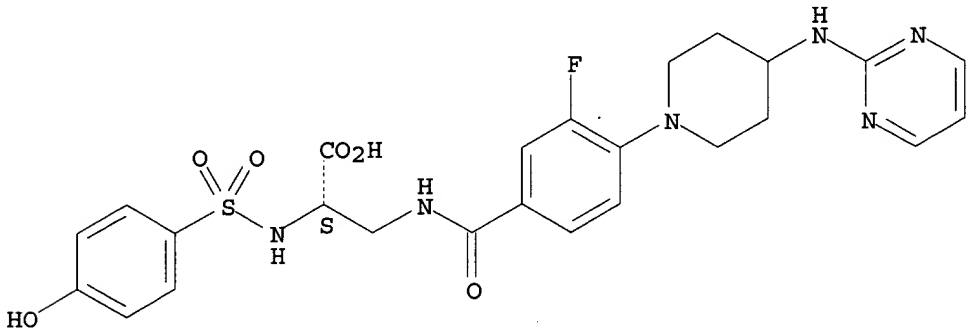
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



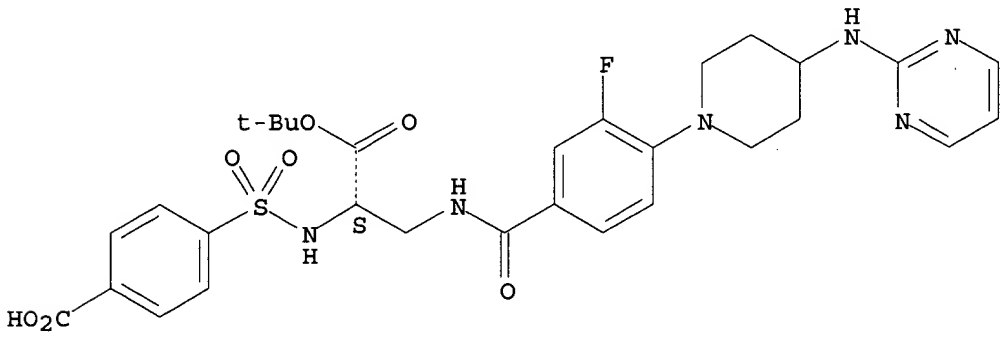
RN 247034-55-5 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-hydroxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



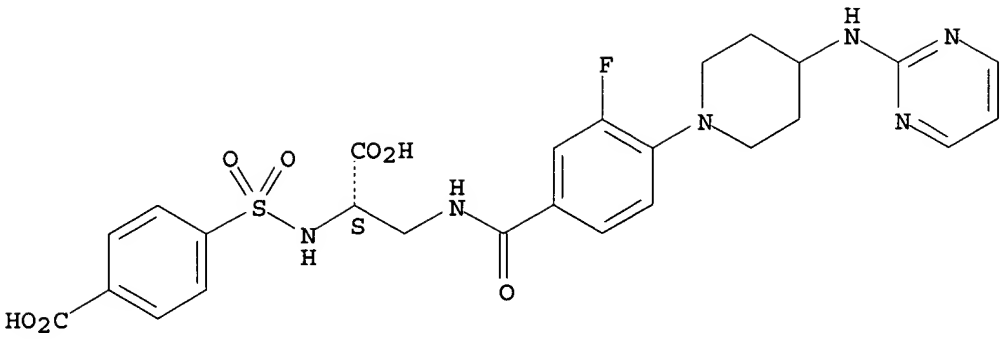
RN 247034-56-6 CAPLUS
CN Benzoic acid, 4-[[[(1S)-2-(1,1-dimethylethoxy)-1-[[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]methyl]-2-oxoethyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



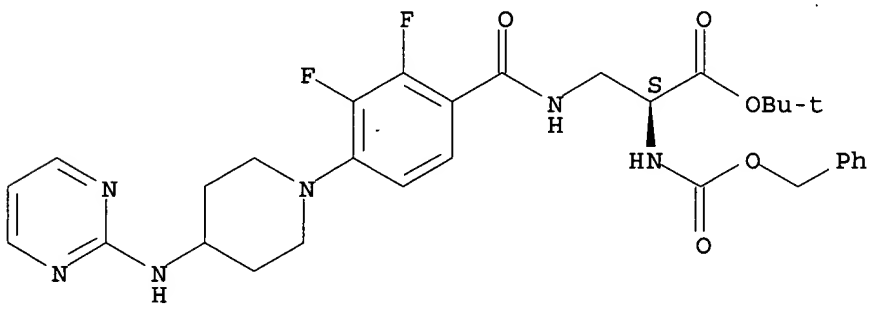
RN 247034-57-7 CAPLUS
CN Benzoic acid, 4-[[[(1S)-1-carboxy-2-[[3-fluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]ethyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



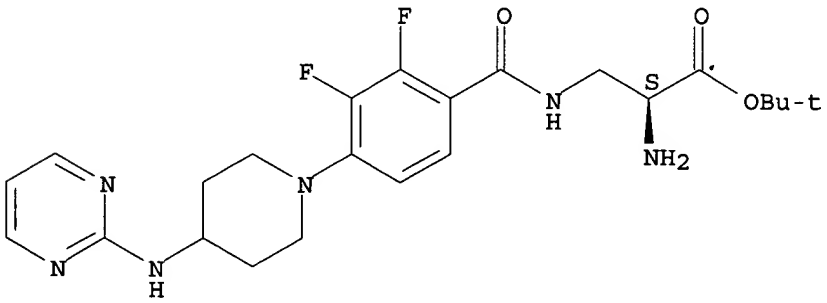
RN 247034-61-3 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



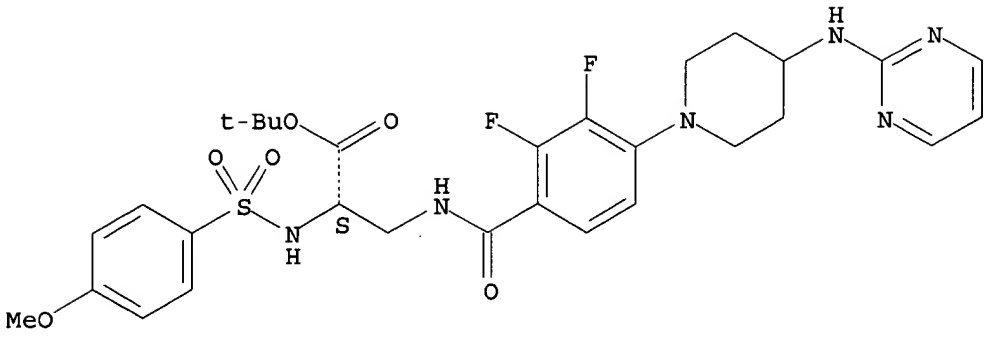
RN 247034-62-4 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



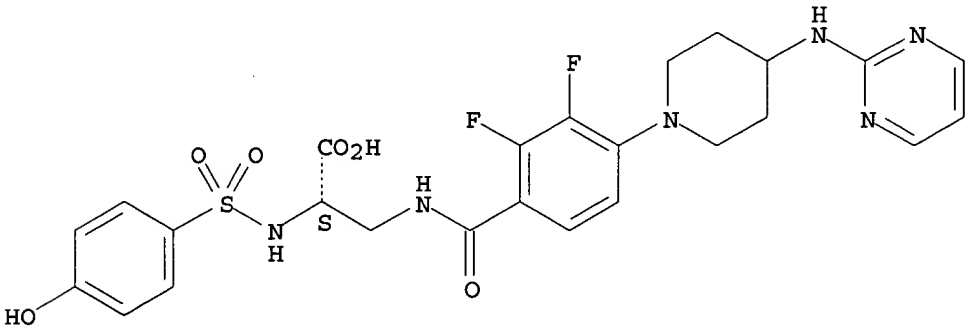
RN 247034-63-5 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-methoxyphenyl)sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



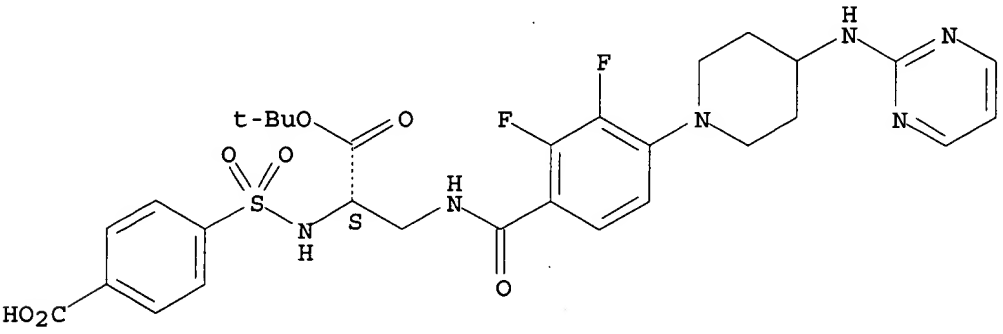
RN 247034-64-6 CAPLUS
CN L-Alanine, 3-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(4-hydroxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 247034-66-8 CAPLUS
CN Benzoic acid, 4-[[[(1S)-1-[[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]methyl]-2-(1,1-dimethylethoxy)-2-oxoethyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)

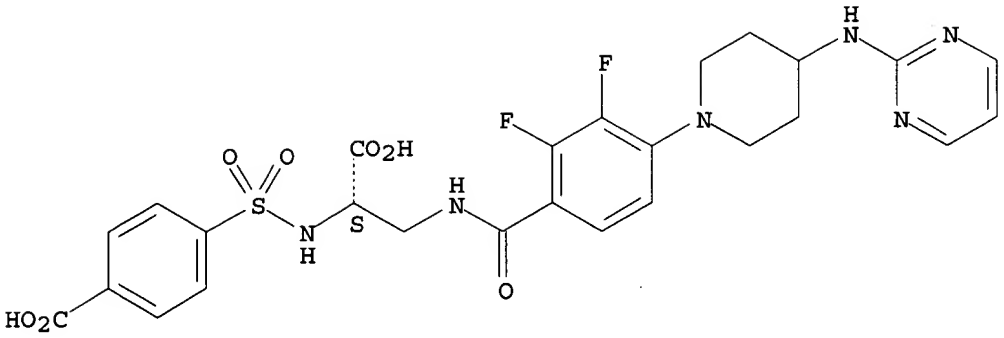
Absolute stereochemistry. Rotation (+).



RN 247034-67-9 CAPLUS
CN Benzoic acid, 4-[[[(1S)-1-carboxy-2-[[2,3-difluoro-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]ethyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)

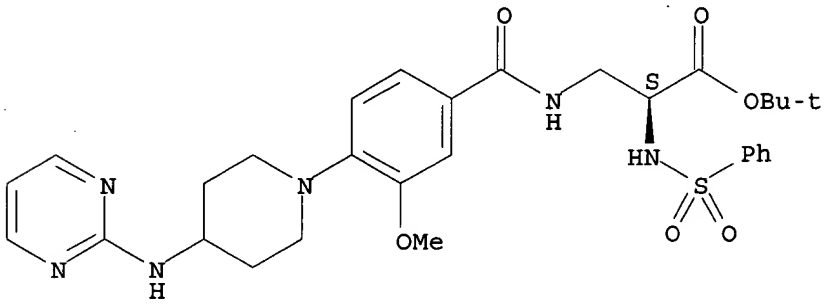
Absolute stereochemistry. Rotation (+).

~~89/ 400,992~~



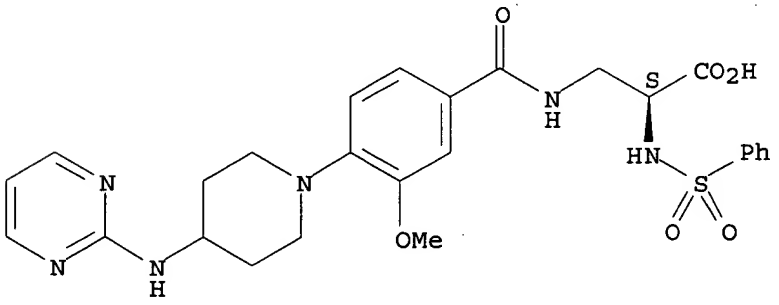
RN 247034-71-5 CAPLUS
CN L-Alanine, 3-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



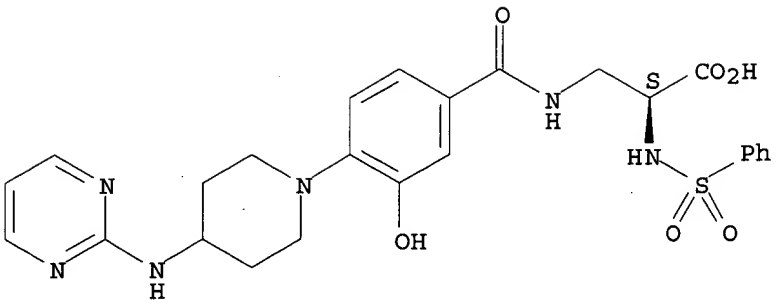
RN 247034-72-6 CAPLUS
CN L-Alanine, 3-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



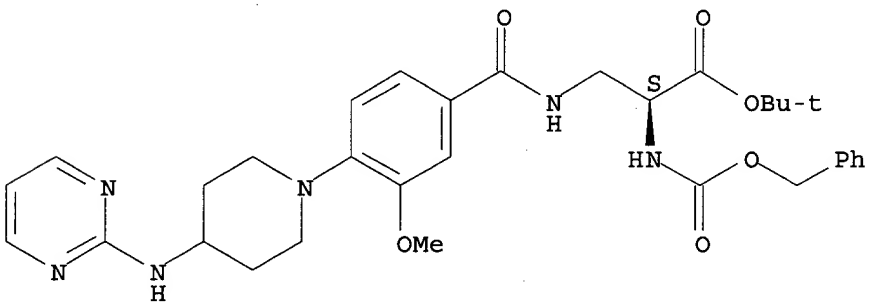
RN 247034-74-8 CAPLUS
CN L-Alanine, 3-[[3-hydroxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



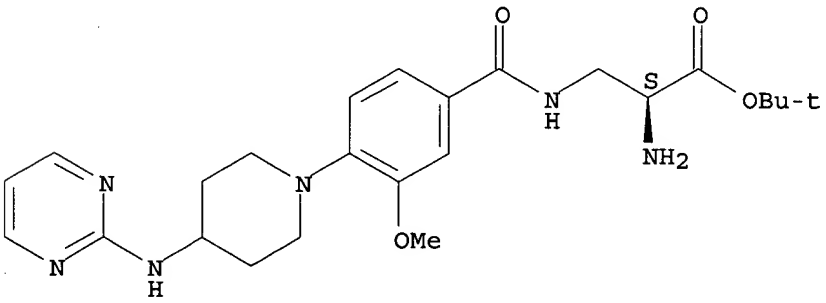
RN 247034-76-0 CAPLUS
CN L-Alanine, 3-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 247034-77-1 CAPLUS
CN L-Alanine, 3-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

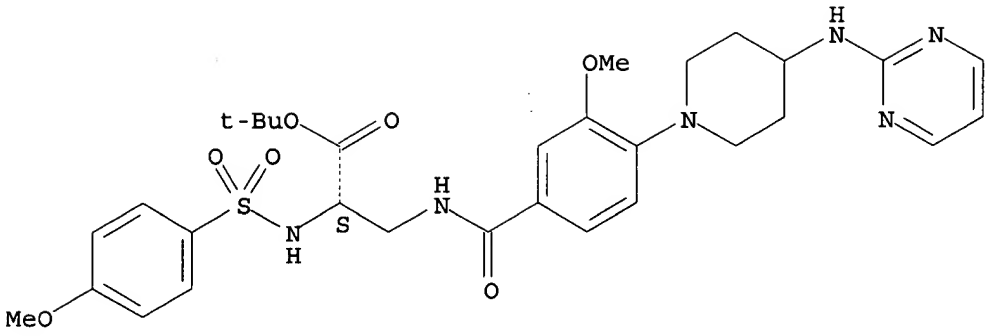
Absolute stereochemistry. Rotation (+).



RN 247034-78-2 CAPLUS
CN L-Alanine, N-[(4-methoxyphenyl)sulfonyl]-3-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

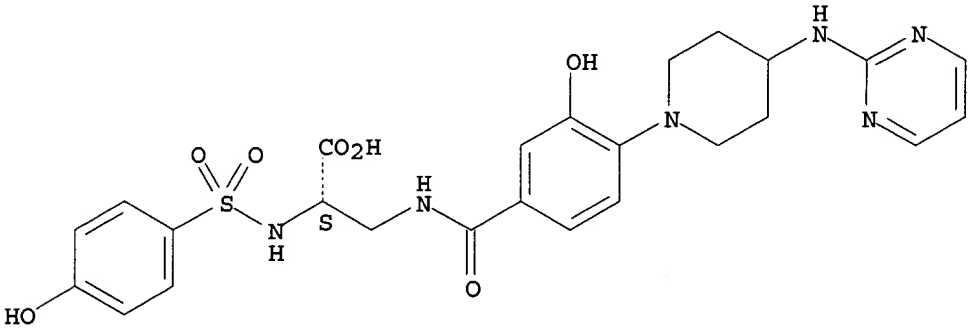
Absolute stereochemistry. Rotation (+).

~~09/400,992~~



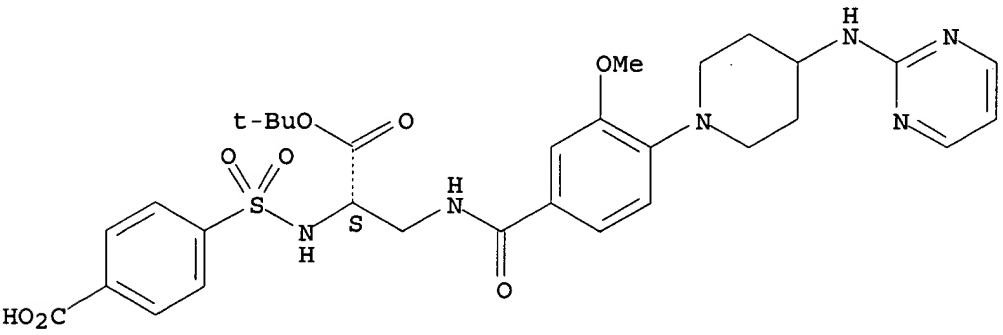
RN 247034-79-3 CAPLUS
CN L-Alanine, N-[(4-hydroxyphenyl)sulfonyl]-3-[[3-hydroxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



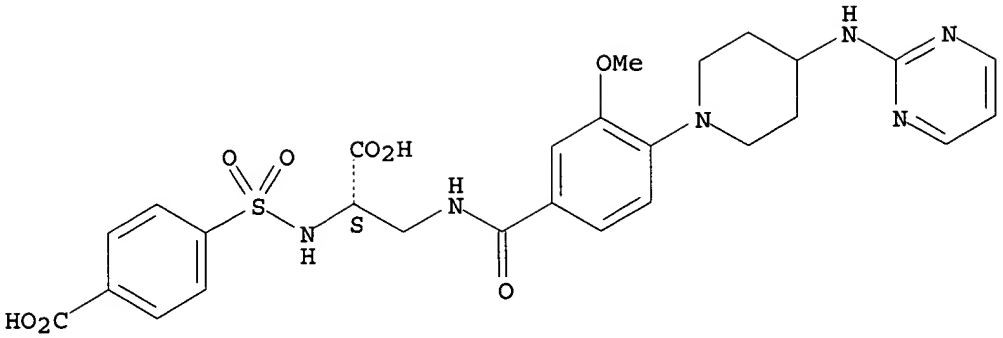
RN 247034-81-7 CAPLUS
CN Benzoic acid, 4-[[[(1S)-2-(1,1-dimethylethoxy)-1-[[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]methyl]-2-oxoethyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



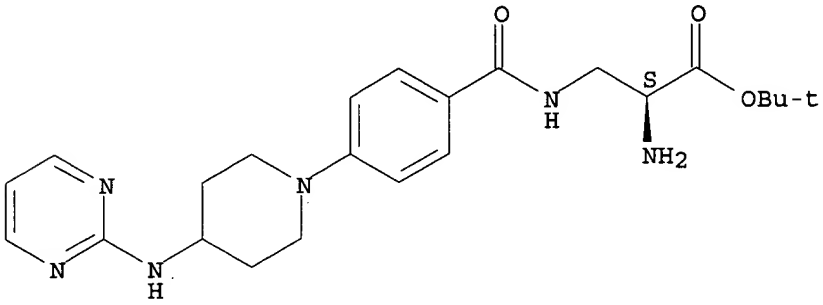
RN 247034-82-8 CAPLUS
CN Benzoic acid, 4-[[[(1S)-1-carboxy-2-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]ethyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



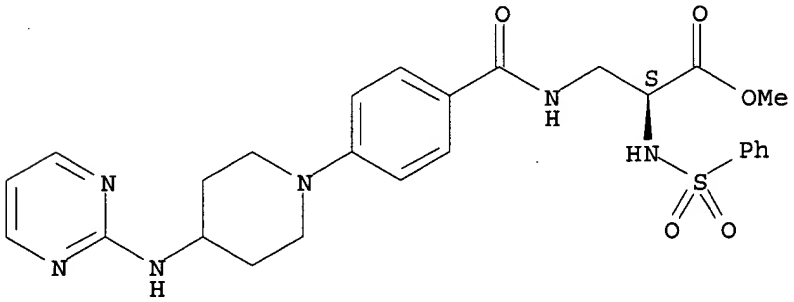
RN 247034-84-0 CAPLUS
CN L-Alanine, 3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 247034-85-1 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:640839 CAPLUS
DOCUMENT NUMBER: 131:271881
TITLE: Preparation of pyrimidinylalkylphenylcarbonylaminopropanoates and related compounds as **integrin** antagonists
INVENTOR(S): Pitts, William J.; Jadhav, Prabhakar K.

~~09/400,992~~

PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Co., USA
SOURCE: PCT Int. Appl., 337 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950249	A2	19991007	WO 1999-US6827	19990329
WO 9950249	A3	19991125		
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2333927	AA	19991007	CA 1999-2333927	19990329
AU 9932137	A1	19991018	AU 1999-32137	19990329
EP 1054871	A2	20001129	EP 1999-914248	19990329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2003504301	T2	20030204	JP 2000-541154	19990329
US 2001044535	A1	20011122	US 2001-828751	20010409
US 6489333	B2	20021203		

PRIORITY APPLN. INFO.: US 1998-80242P P 19980401
WO 1999-US6827 W 19990329
US 1999-282496 A3 19990331

OTHER SOURCE(S): MARPAT 131:271881

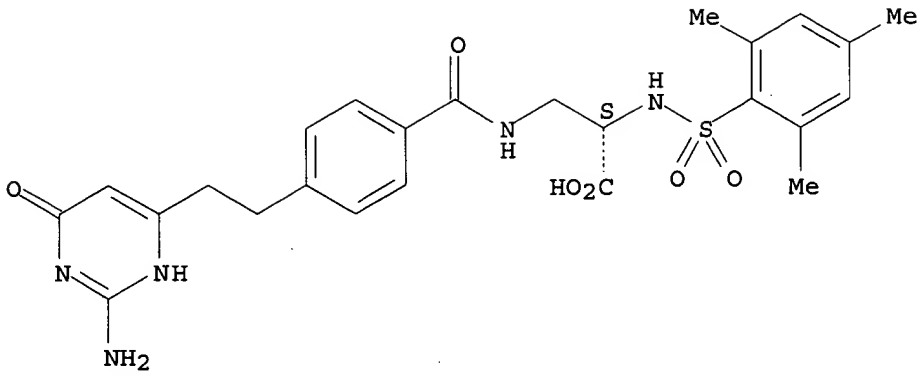
AB GT (T = **integrin** antagonist template; G = specified guanidine mimic), were prepd. as antagonists of the .alpha.v.beta.3 **integrin**, the .alpha.2b.beta.3 **integrin**, and related cell surface adhesive protein receptors for the inhibition of cell adhesion, treatment of angiogenic disorders, inflammation, bone degrdn., cancer metastasis, diabetic retinopathy, thrombosis, restenosis, macular degeneration, and other conditions mediated by cell adhesion and/or cell migration and/or angiogenesis. Thus, 2-[(S)-2,4,6-trimethylphenylsulfonylamino]-3-[4-[2-(2,4-diaminopyrimidin-6-yl)ethyl]phenylcarbonylamino]propionic acid trifluoroacetate was prepd. in several steps from L-asparagine. In the .alpha.v.beta.3-vitronectin assay, tested title compds. showed IC50.ltoreq.10 .mu.M.

IT **245527-29-1P 245527-30-4P 245527-32-6P**
245527-33-7P 245527-36-0P 245527-37-1P
245527-38-2P 245527-40-6P 245527-41-7P
245527-42-8P 245527-44-0P 245527-46-2P
245527-49-5P 245527-51-9P 245527-53-1P
245527-65-5P 245527-67-7P 245527-69-9P
245527-72-4P 245527-74-6P 245527-76-8P
245527-78-0P 245528-21-6P 245528-33-0P
245528-40-9P 245528-62-5P 245528-69-2P
245528-71-6P 245528-74-9P 245528-75-0P
245528-76-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of pyrimidinylalkylphenylcarbonylaminopropanoates and related compds. as **integrin** antagonists)

RN 245527-29-1 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

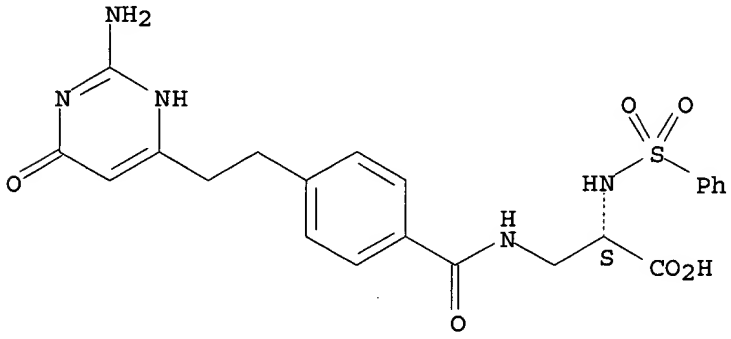
~~09/400,992~~



● Na

RN 245527-30-4 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-(phenylsulfonyl)-, monosodium salt (9CI) (CA INDEX NAME)

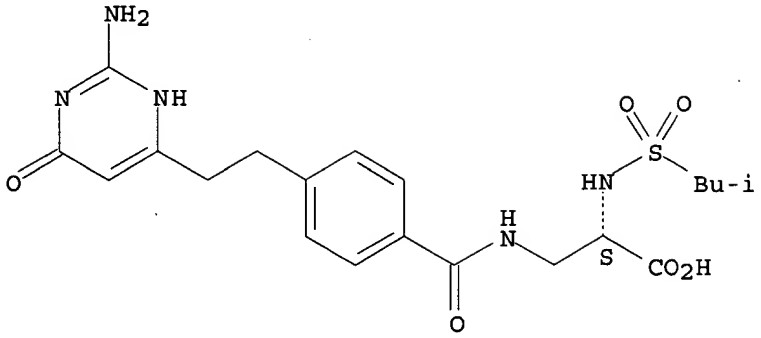
Absolute stereochemistry.



● Na

RN 245527-32-6 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2-methylpropyl)sulfonyl]-, monosodium salt (9CI) (CA INDEX NAME)

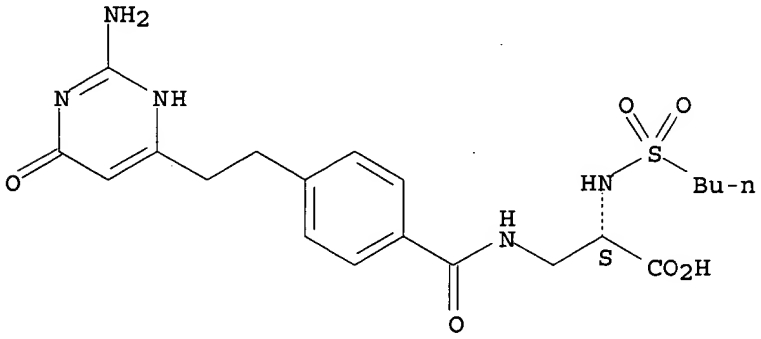
Absolute stereochemistry.



● Na

RN 245527-33-7 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-(butylsulfonyl)-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

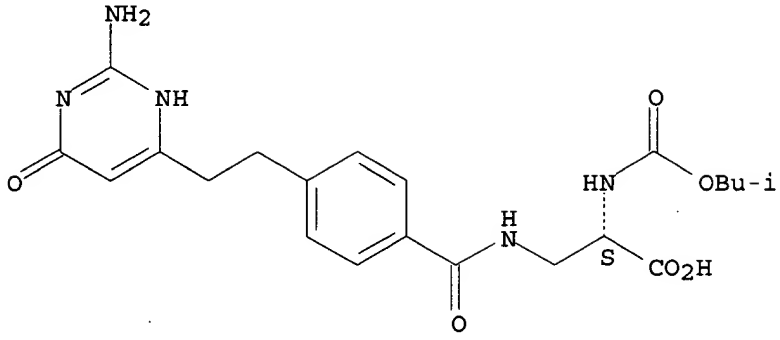


● Na

RN 245527-36-0 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2-methylpropoxy)carbonyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

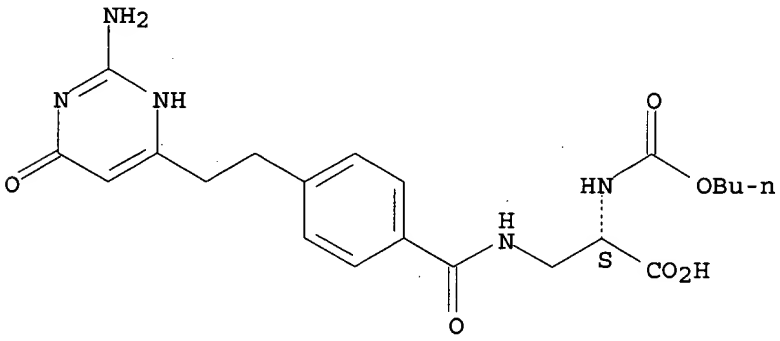
~~09/400,992~~



● Na

RN 245527-37-1 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-(butoxycarbonyl)-, monosodium salt (9CI) (CA INDEX NAME)

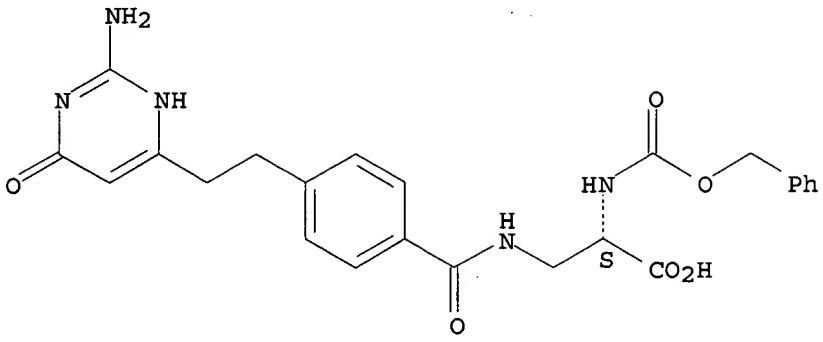
Absolute stereochemistry.



● Na

RN 245527-38-2 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



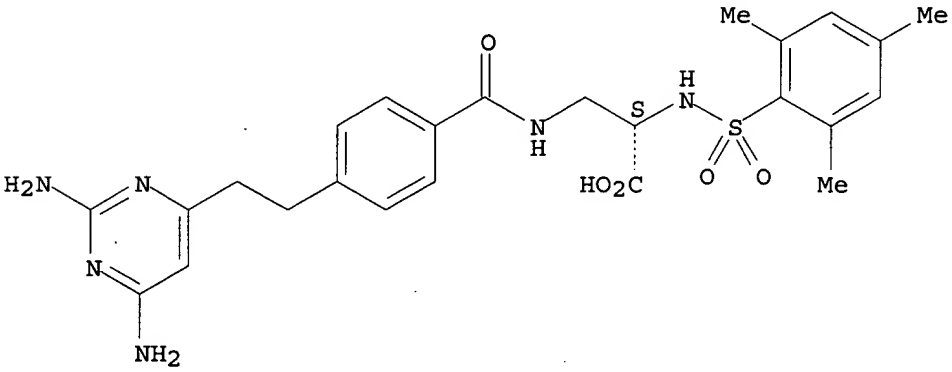
● Na

RN 245527-40-6 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

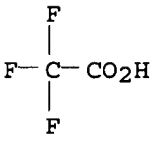
CRN 245527-39-3
CMF C25 H30 N6 O5 S

Absolute stereochemistry.



CM 2

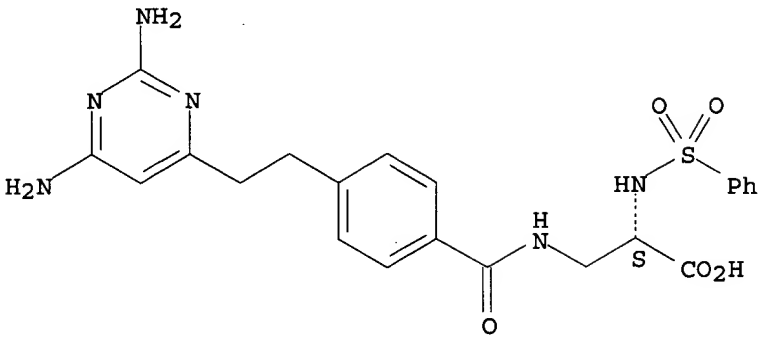
CRN 76-05-1
CMF C2 H F3 O2



RN 245527-41-7 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

~~09/ 400,992~~

Absolute stereochemistry.

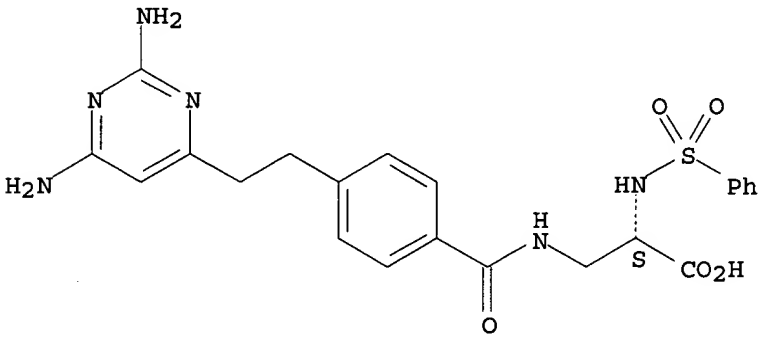


RN 245527-42-8 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

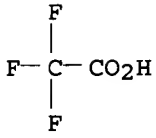
CRN 245527-41-7
CMF C22 H24 N6 O5 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 245527-44-0 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2-methylpropyl)sulfonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

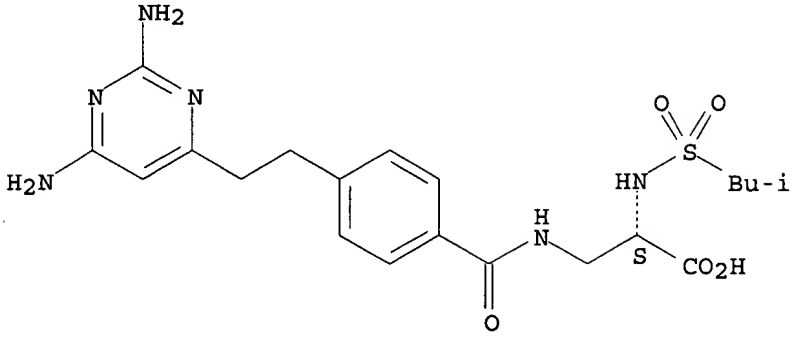
CM 1

CRN 245527-43-9

~~09/400,992~~

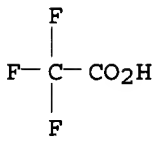
CMF C20 H28 N6 O5 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

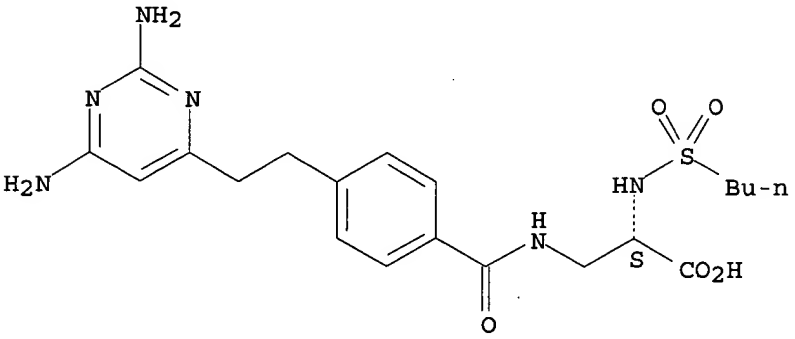


RN 245527-46-2 CAPLUS
CN L-Alanine, N-(butylsulfonyl)-3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

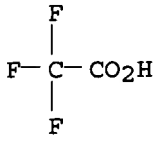
CRN 245527-45-1
CMF C20 H28 N6 O5 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

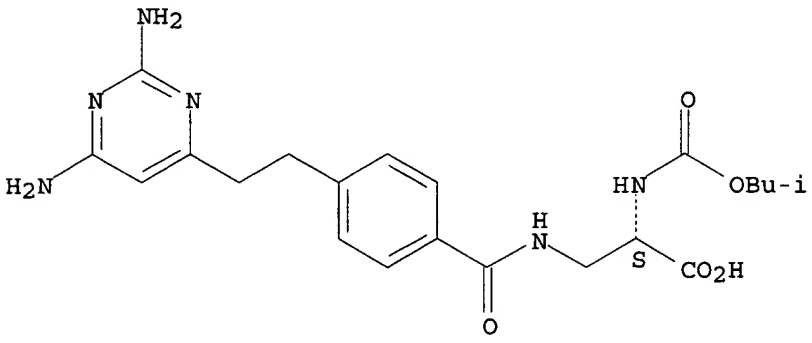


RN 245527-49-5 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2-methylpropoxy)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

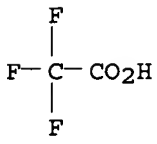
CRN 245527-48-4
CMF C21 H28 N6 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



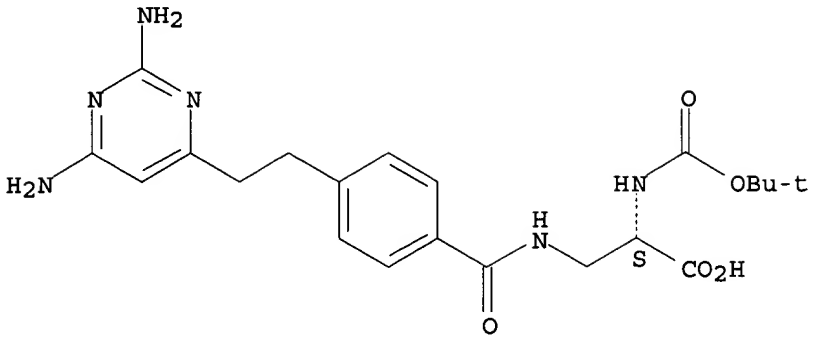
RN 245527-51-9 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(1,1-dimethylethoxy)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 245527-50-8
CMF C21 H28 N6 O5

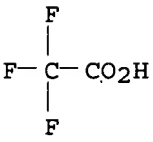
Absolute stereochemistry.

~~09/400,992~~



CM 2

CRN 76-05-1
CMF C2 H F3 O2

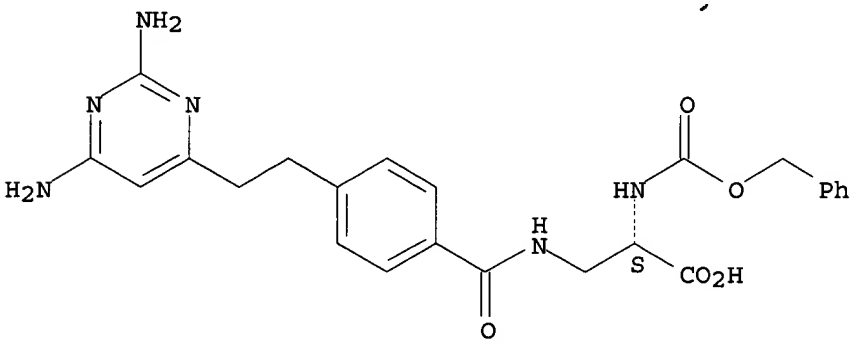


RN 245527-53-1 CAPLUS
CN L-Alanine, 3-[[4-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

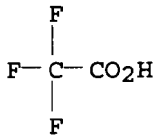
CRN 245527-52-0
CMF C24 H26 N6 O5

Absolute stereochemistry.



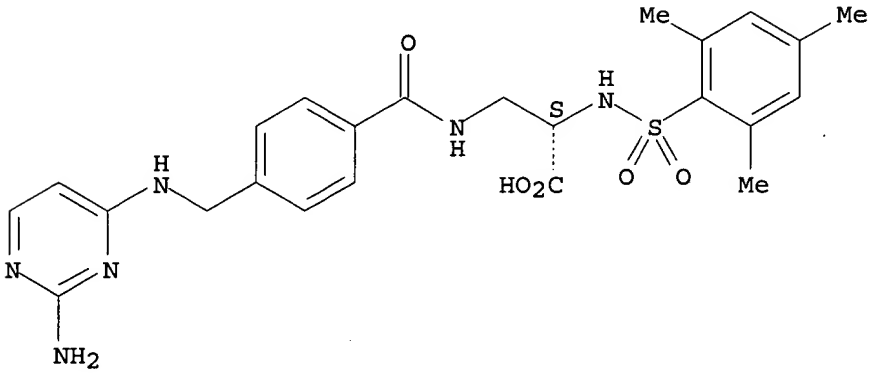
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 245527-65-5 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

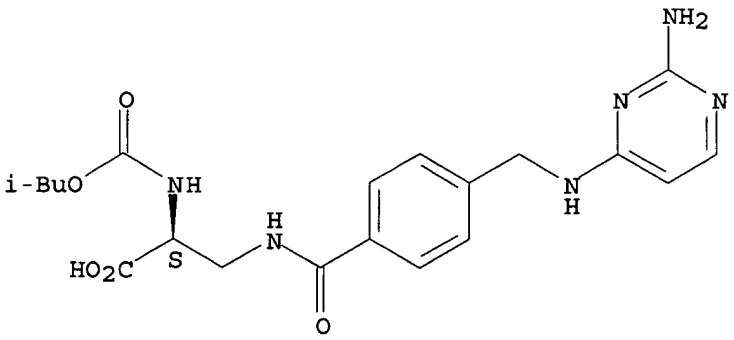


RN 245527-67-7 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-[(2-methylpropoxy)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

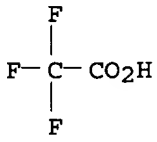
CRN 245527-66-6
CMF C20 H26 N6 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

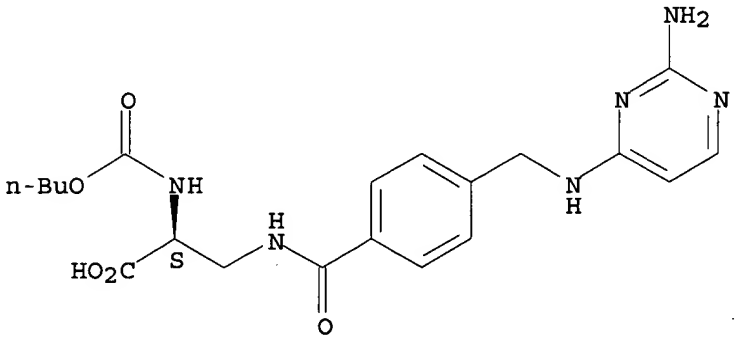


RN 245527-69-9 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-(butoxycarbonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

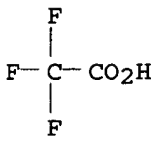
CRN 245527-68-8
CMF C20 H26 N6 O5

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



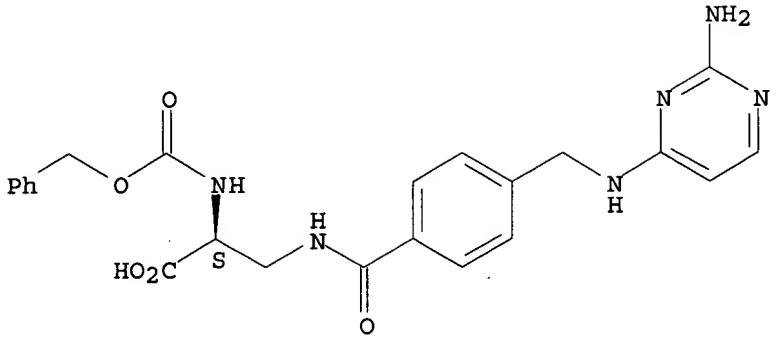
RN 245527-72-4 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 245527-71-3
CMF C23 H24 N6 O5

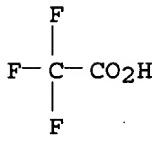
Absolute stereochemistry.

~~09/400,992~~



CM 2

CRN 76-05-1
CMF C2 H F3 O2

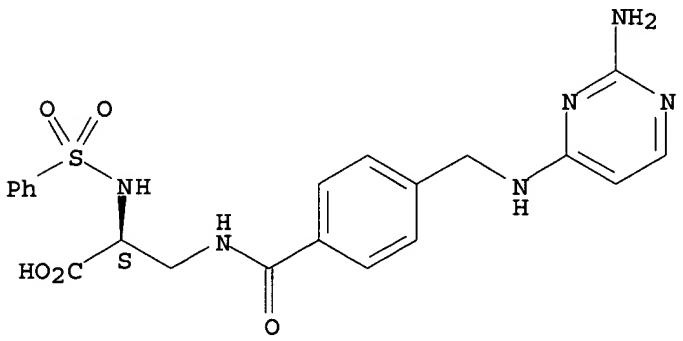


RN 245527-74-6 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-(phenylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 245527-73-5
CMF C21 H22 N6 O5 S

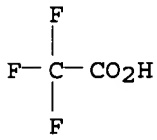
Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

~~09/400,992~~

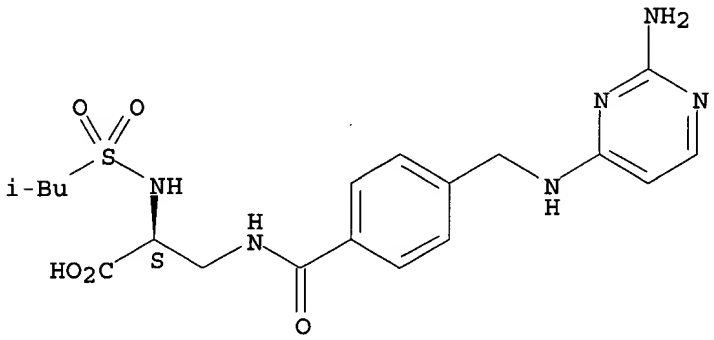


RN 245527-76-8 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-[(2-methylpropyl)sulfonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

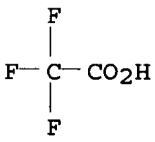
CRN 245527-75-7
CMF C19 H26 N6 O5 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

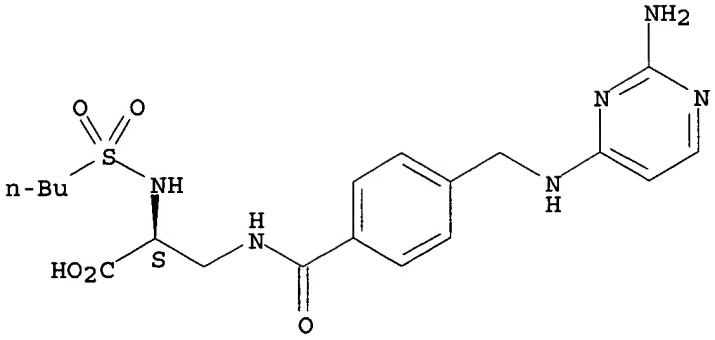


RN 245527-78-0 CAPLUS
CN L-Alanine, 3-[[4-[[(2-amino-4-pyrimidinyl)amino]methyl]benzoyl]amino]-N-(butylsulfonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

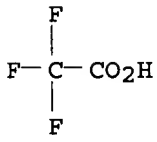
CRN 245527-77-9
CMF C19 H26 N6 O5 S

Absolute stereochemistry.



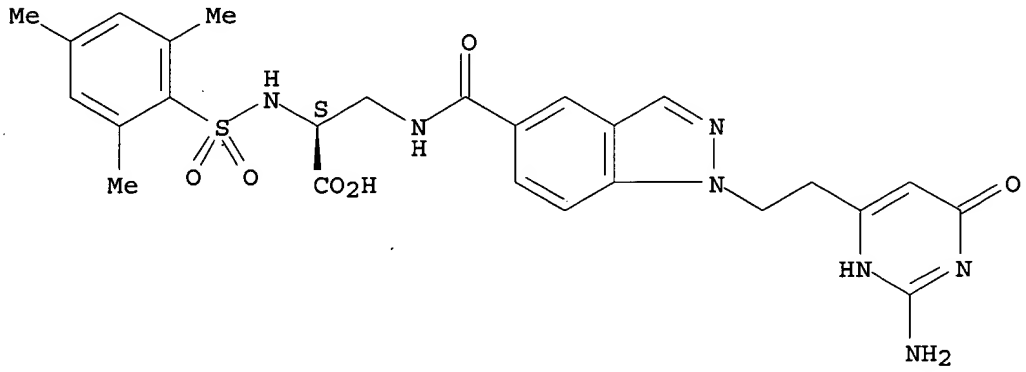
CM 2

CRN 76-05-1
CMF C2 H F3 O2



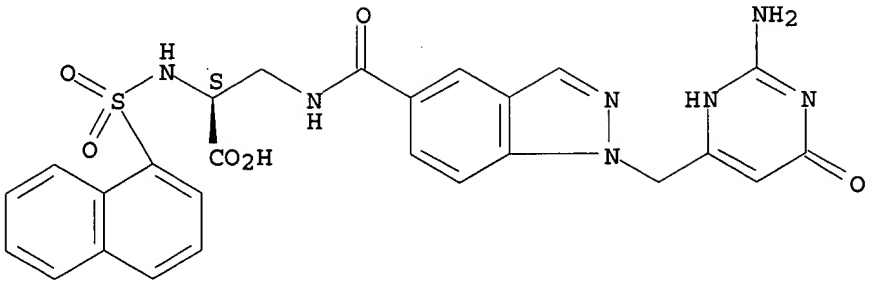
RN 245528-21-6 CAPLUS
CN L-Alanine, 3-[[[1-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]-1H-indazol-5-yl]carbonyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



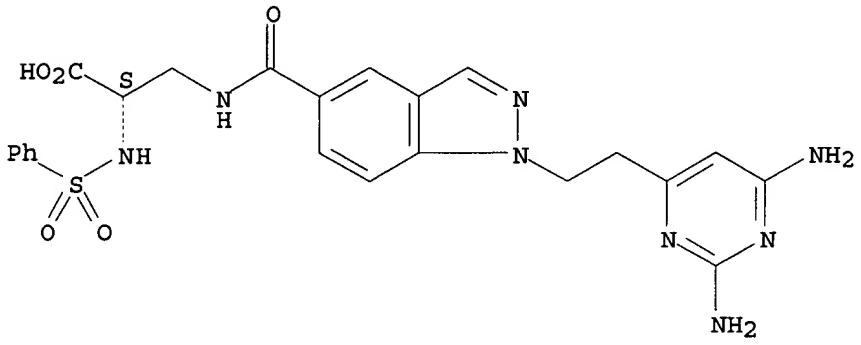
RN 245528-33-0 CAPLUS
CN L-Alanine, 3-[[[1-[(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)methyl]-1H-indazol-5-yl]carbonyl]amino]-N-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



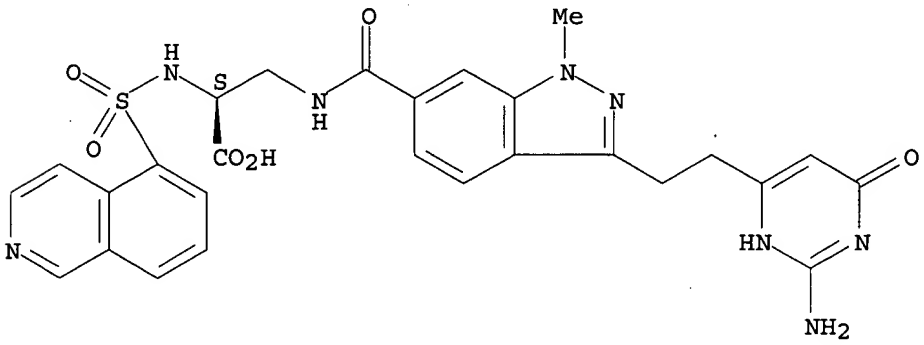
RN 245528-40-9 CAPLUS
CN L-Alanine, 3-[[[1-[2-(2,6-diamino-4-pyrimidinyl)ethyl]-1H-indazol-5-yl]carbonyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 245528-62-5 CAPLUS
CN L-Alanine, 3-[[[3-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]-1-methyl-1H-indazol-6-yl]carbonyl]amino]-N-(5-isoquinolinylsulfonyl)- (9CI) (CA INDEX NAME)

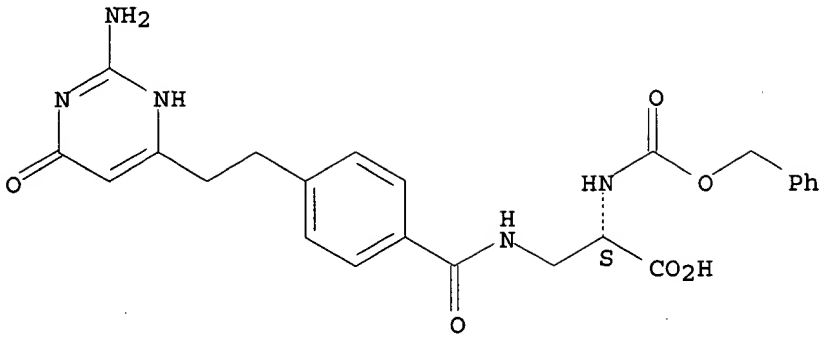
Absolute stereochemistry.



RN 245528-69-2 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

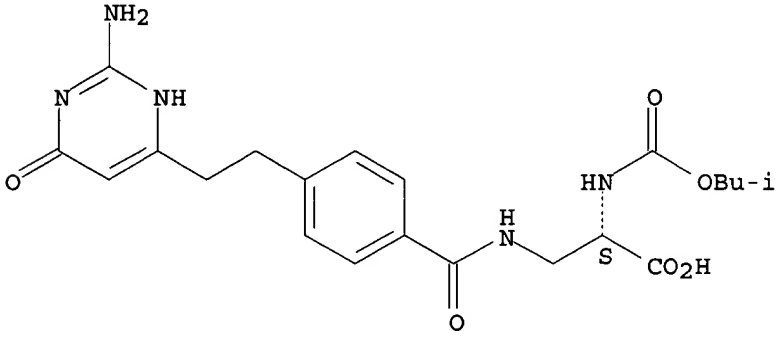
Absolute stereochemistry.

~~09/400,992~~



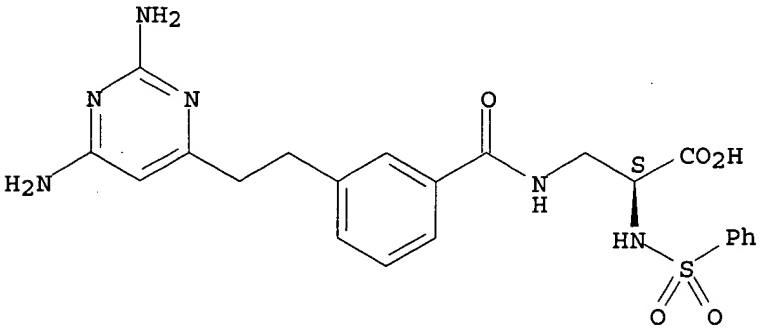
RN 245528-71-6 CAPLUS
CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2-methylpropoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 245528-74-9 CAPLUS
CN L-Alanine, 3-[[3-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

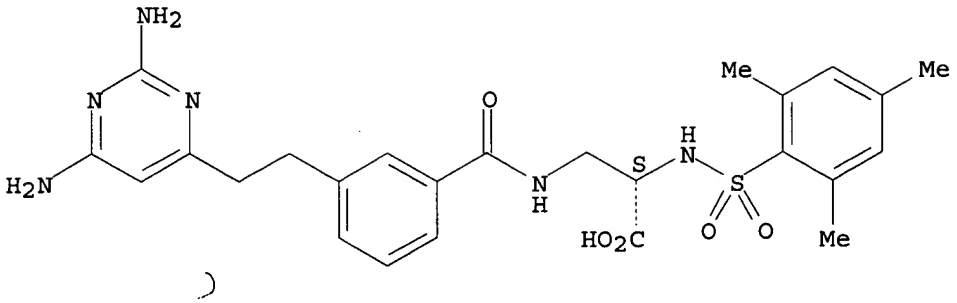
Absolute stereochemistry.



RN 245528-75-0 CAPLUS
CN L-Alanine, 3-[[3-[2-(2,6-diamino-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

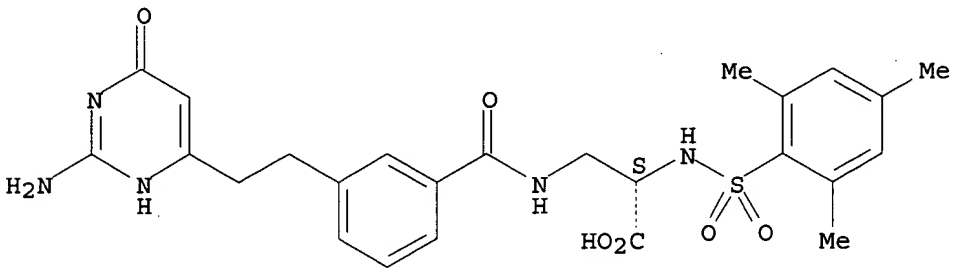
Absolute stereochemistry.

~~09/400,992~~



RN 245528-76-1 CAPLUS
CN L-Alanine, 3-[[3-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:495277 CAPLUS
DOCUMENT NUMBER: 131:130008
TITLE: Preparation of phenylpiperazine derivatives as **integrin** .alpha.v.beta.3 antagonists
INVENTOR(S): Ajito, Keiichi; Murakami, Shoichi; Ishikawa, Minoru; Yamamoto, Mikio; Kubota, Dai; Gomi, Shuichi; Hachisu, Mitsugu; Katano, Kiyoaki
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9938849	A1	19990805	WO 1999-JP415	19990201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319824	AA	19990805	CA 1999-2319824	19990201
AU 9920762	A1	19990816	AU 1999-20762	19990201
EP 1057818	A1	20001206	EP 1999-901205	19990201

~~09/400,992~~

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

US 6451800 B1 20020917 US 2000-601176 20000728

PRIORITY APPLN. INFO.: JP 1998-19282 A 19980130

WO 1999-JP415 W 19990201

OTHER SOURCE(S): MARPAT 131:130008

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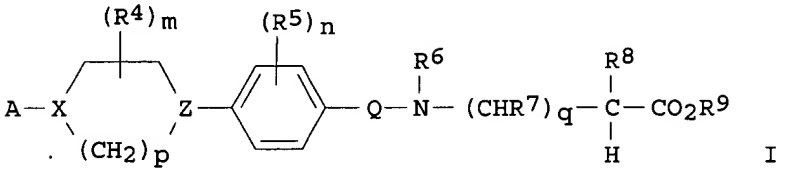

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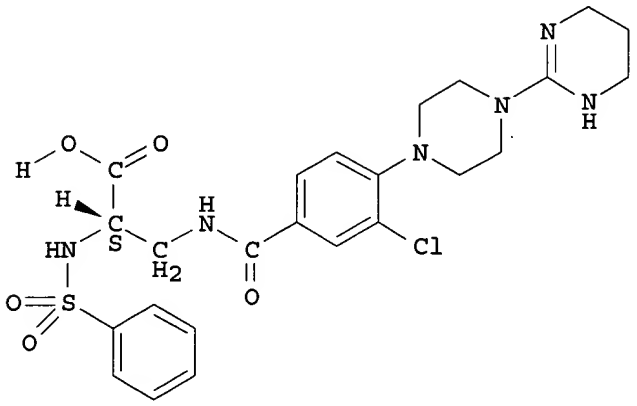


II

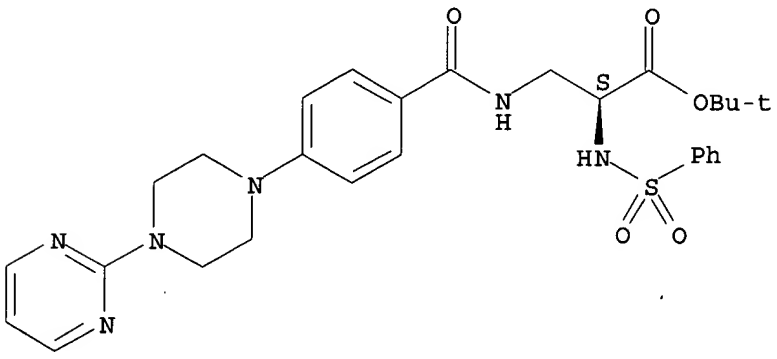
AB Compds. represented by general formula (I) or pharmaceutically acceptable salts or solvates thereof [A = (un)satd. and (un)satd. 5- to 7-membered heterocycle contg. two nitrogen atoms, optionally fused to (un)satd. and (un)satd. 5- to 7-membered heterocycle, (un)substituted C(:NH)NH2; X, Z = CH, N; R4, R5 = (un)substituted C1-6 alkyl or alkoxy, halogeno, NH2, NO2, OH; Q CO, CH2, CHR10, CHOR10; wherein R10 = C1-6 alkyl; R6 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl or alkynyl, (un)substituted aralkyl; R7 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl or alkynyl, aralkyl, or NH2 ; R8 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, or C2-6 alkynyl, (un)substituted aralkyl or NH2; R9 = H, alkyl; m = 0 to 5; n = 0 to 4; p = 2 or 3; q = 0 or 1] are prepd. These compds. also exhibit potent antagonizing effect on blood platelet membrane protein GP IIb/IIa and potent inhibiting-effect on human blood platelet aggregation and are useful for the treatment of **integrin** .alpha.v.beta.3-mediated diseases such as cardiovascular diseases, neovascularization-related diseases, cancer or its metastasis, immune diseases, or bone diseases and useful as blood platelet aggregation inhibitors for the treatment of blood platelet thrombosis, thromboembolism, thrombocytopenic purpura, and hemolytic uremic syndrome, for improving peripheral blood circulation, and for inhibiting blood aggregation during exo-circulation. Thus, Me 2-chloro-4-(piperazin-1-yl)benzoate was condensed with 2-bromopyridine in the presence of (Me2CH)2NEt in DMF at 80.degree. for 5.0 h, followed by sapon. with a mixt. of 1 N NaOH, MeOH, and THF and acidification with 1 N HCl to give the title compd. (II). In a **integrin** .alpha.v.beta.3 binding assay, II in vitro showed IC50 of 3.5 nM .mu.g/mL for inhibiting the binding of vitronectin to vitronectin receptors.

IT **234080-72-9P 234080-73-0P 234080-75-2P**

234080-76-3P 234080-78-5P 234080-79-6P
234080-81-0P 234080-82-1P 234080-84-3P
234080-85-4P 234080-89-8P 234080-91-2P
234080-92-3P 234080-93-4P 234080-95-6P
234080-97-8P 234080-99-0P 234081-00-6P
234081-04-0P 234081-05-1P 234081-08-4P
234081-09-5P 234081-14-2P 234081-15-3P
234081-18-6P 234081-19-7P 234081-21-1P
234081-22-2P 234081-25-5P 234081-26-6P
234081-28-8P 234081-29-9P 234081-31-3P
234081-32-4P 234081-34-6P 234081-35-7P
234081-37-9P 234081-38-0P 234081-40-4P
234081-41-5P 234081-44-8P 234081-45-9P
234081-47-1P 234081-48-2P 234081-52-8P
234081-54-0P 234081-58-4P 234081-60-8P
234081-62-0P 234081-66-4P 234081-68-6P
234081-70-0P 234081-71-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of phenylpiperazine derivs. as **integrin** .alpha.v.beta.3 antagonists and blood platelet aggregation inhibitors for treatment of diseases)

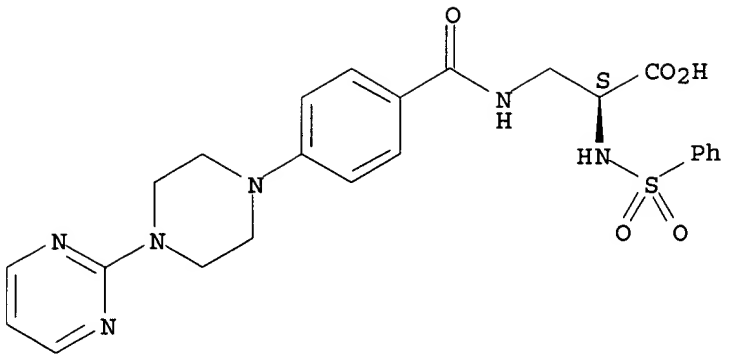
RN 234080-72-9 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



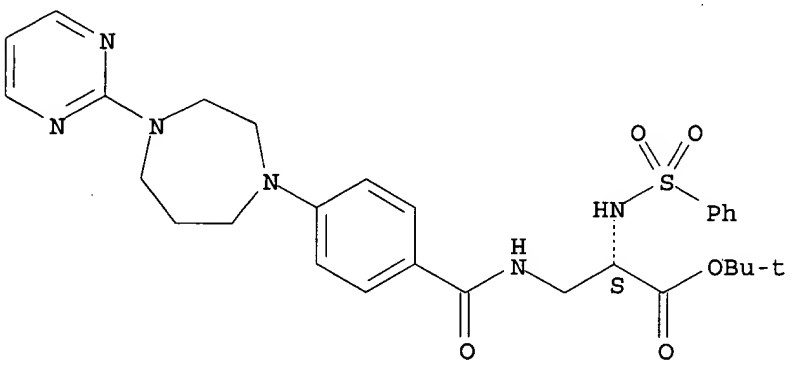
RN 234080-73-0 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



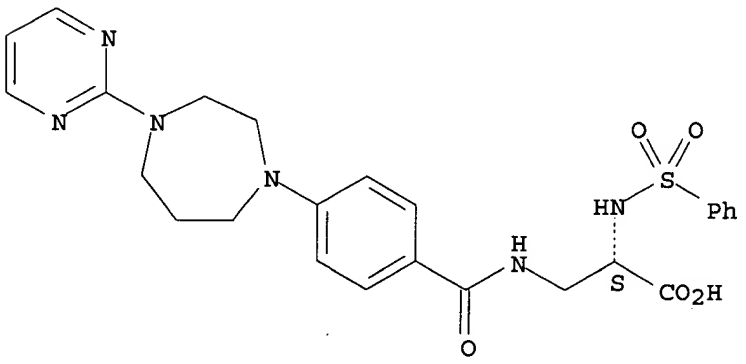
RN 234080-75-2 CAPLUS
CN L-Alanine, 3-[[4-[hexahydro-4-(2-pyrimidinyl)-1H-1,4-diazepin-1-yl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234080-76-3 CAPLUS
CN L-Alanine, 3-[[4-[hexahydro-4-(2-pyrimidinyl)-1H-1,4-diazepin-1-yl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

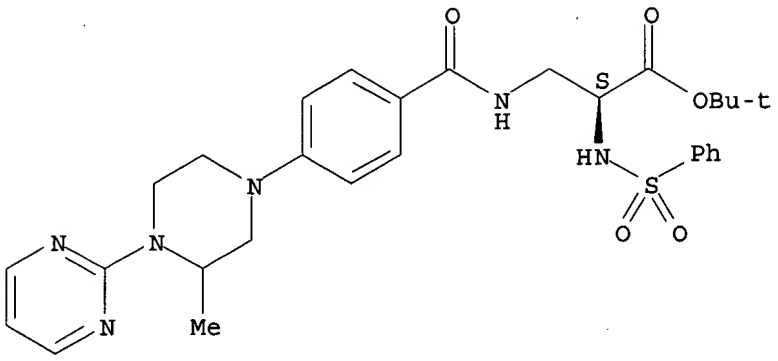
Absolute stereochemistry.



RN 234080-78-5 CAPLUS
CN L-Alanine, 3-[[4-[3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

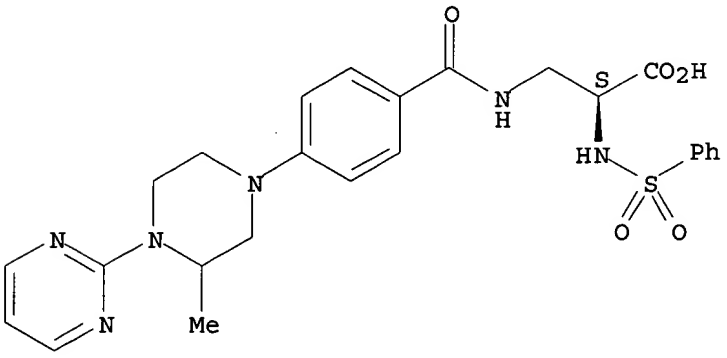
~~09/400,992~~

Absolute stereochemistry.



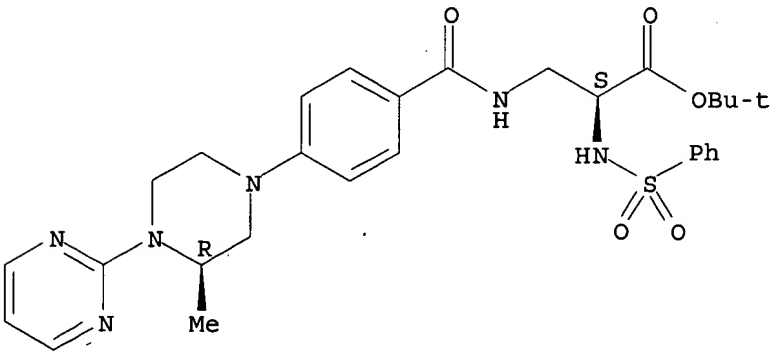
RN 234080-79-6 CAPLUS
CN L-Alanine, 3-[[4-[3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



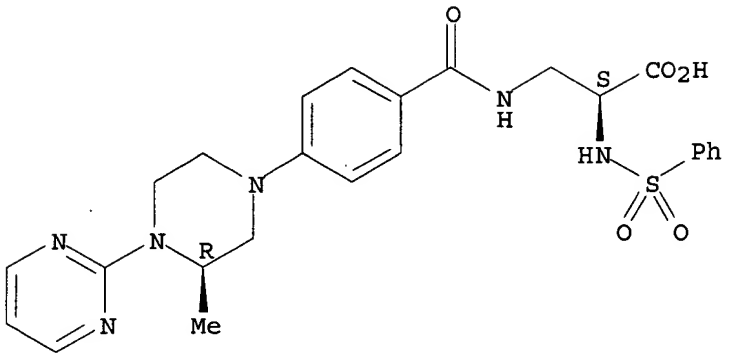
RN 234080-81-0 CAPLUS
CN L-Alanine, 3-[[4-[(3R)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



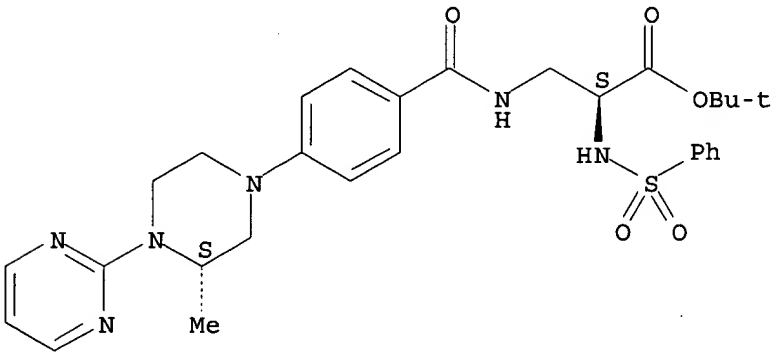
RN 234080-82-1 CAPLUS
CN L-Alanine, 3-[[4-[(3R)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



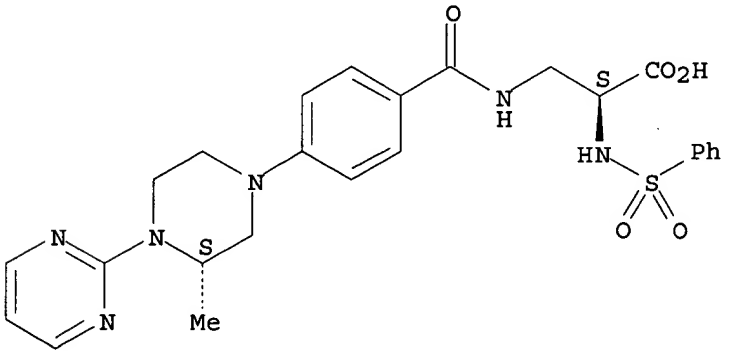
RN 234080-84-3 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234080-85-4 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

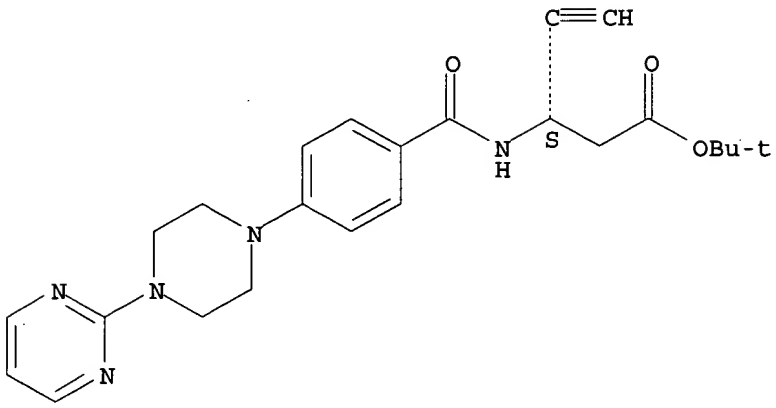
Absolute stereochemistry.



RN 234080-89-8 CAPLUS
CN 4-Pentynoic acid, 3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-,

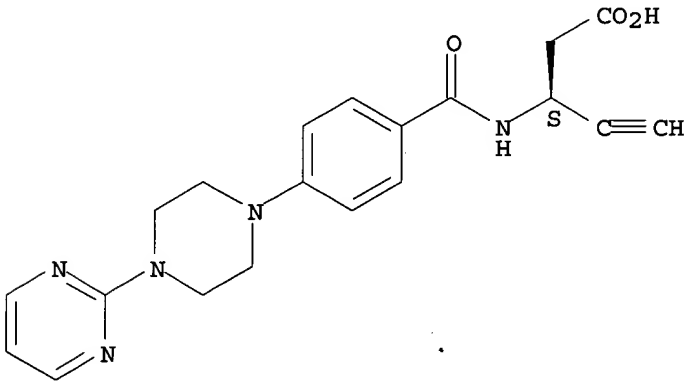
1,1-dimethylethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



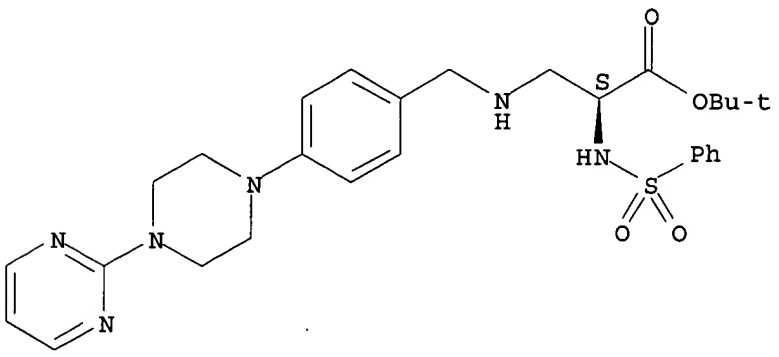
RN 234080-91-2 CAPLUS
CN 4-Pentynoic acid, 3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



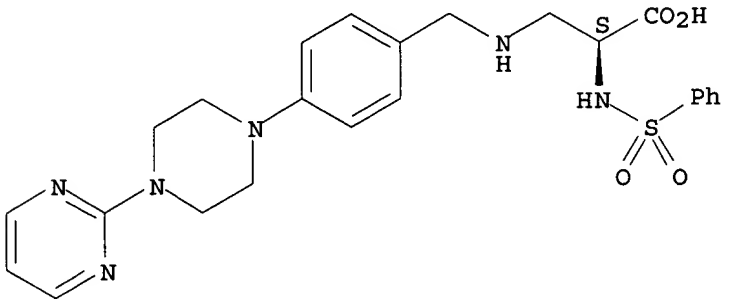
RN 234080-92-3 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[4-[4-(2-pyrimidinyl)-1-piperazinyl]phenyl]methyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



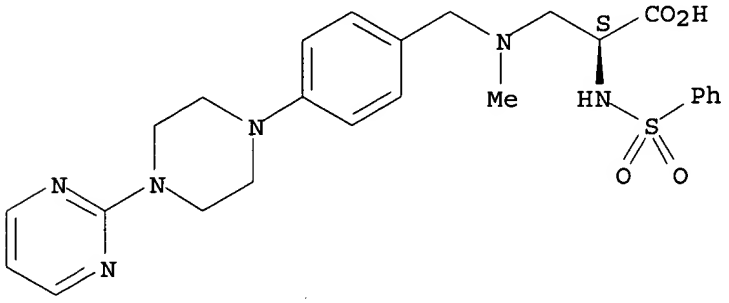
RN 234080-93-4 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[4-[4-(2-pyrimidinyl)-1-piperazinyl]phenyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



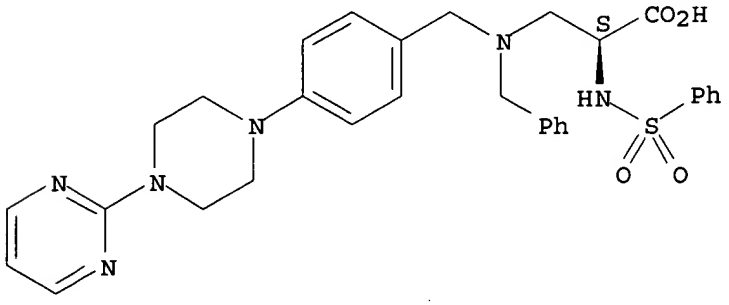
RN 234080-95-6 CAPLUS
CN L-Alanine, 3-[methyl[[4-[4-(2-pyrimidinyl)-1-piperazinyl]phenyl]methyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



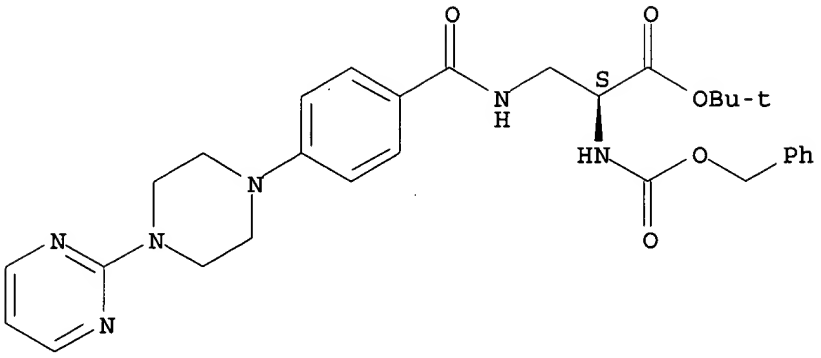
RN 234080-97-8 CAPLUS
CN L-Alanine, 3-[(phenylmethyl)[[4-[4-(2-pyrimidinyl)-1-piperazinyl]phenyl]methyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



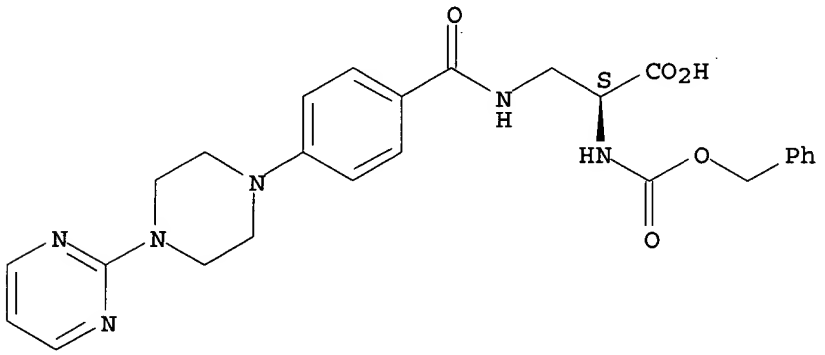
RN 234080-99-0 CAPLUS
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



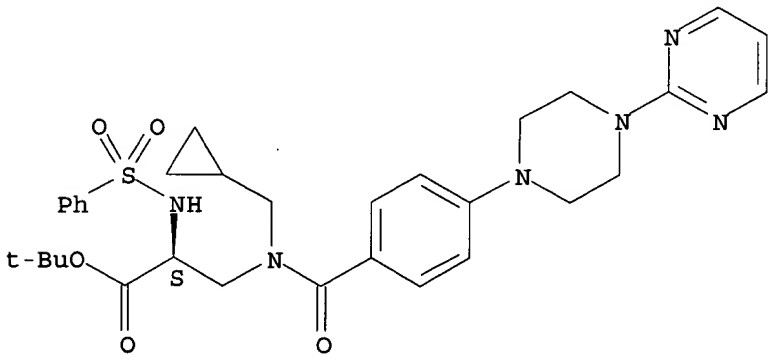
RN 234081-00-6 CAPLUS
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-04-0 CAPLUS
CN L-Alanine, 3-[(cyclopropylmethyl)[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

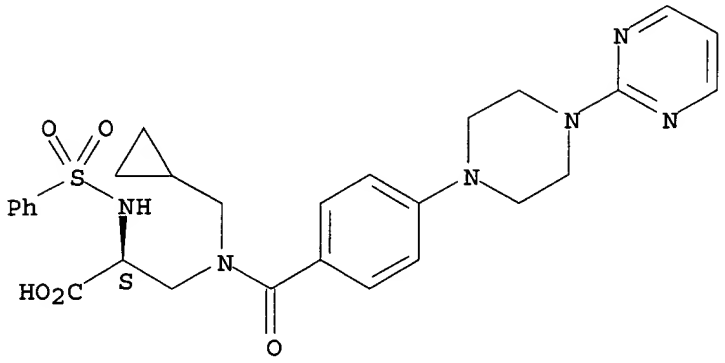
Absolute stereochemistry.



RN 234081-05-1 CAPLUS
CN L-Alanine, 3-[(cyclopropylmethyl)[4-[4-(2-pyrimidinyl)-1-

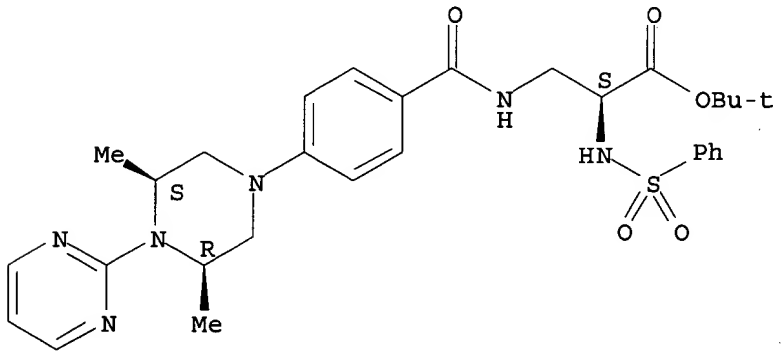
piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



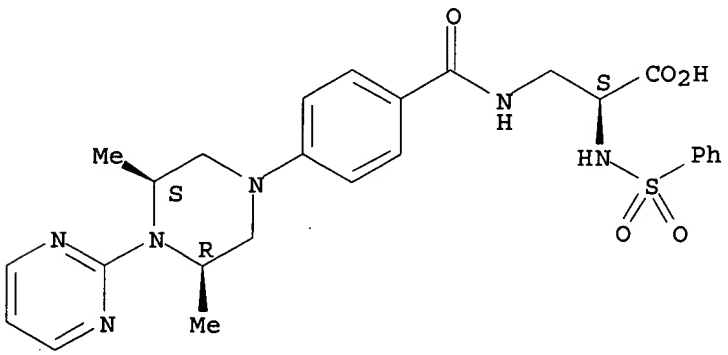
RN 234081-08-4 CAPLUS
CN D-Alanine, 3-[[4-[(3R,5S)-3,5-dimethyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 234081-09-5 CAPLUS
CN D-Alanine, 3-[[4-[(3R,5S)-3,5-dimethyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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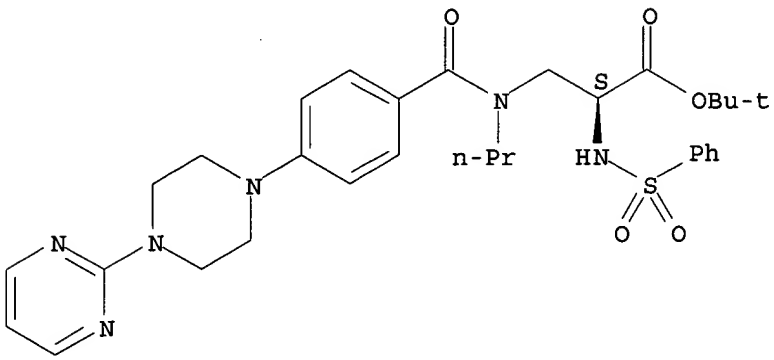
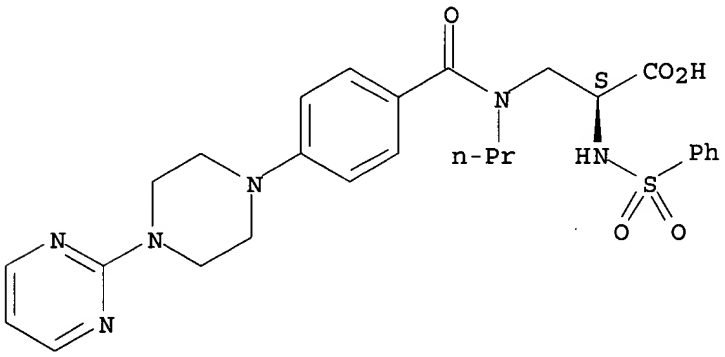
RN 234081-14-2 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[propyl[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-15-3 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[propyl[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

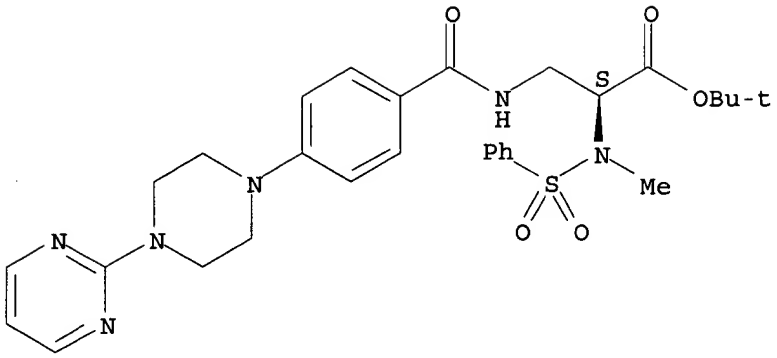
Absolute stereochemistry.



RN 234081-18-6 CAPLUS
CN L-Alanine, N-methyl-N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

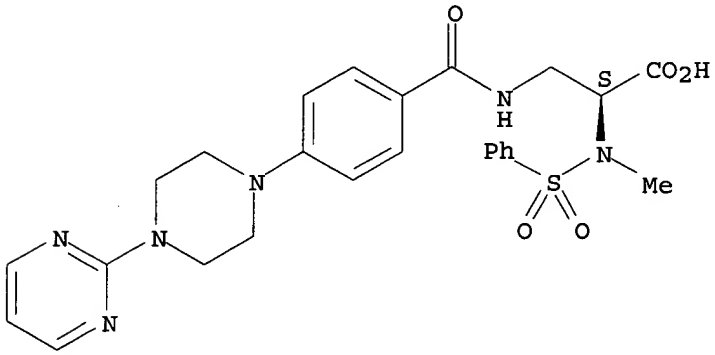
Absolute stereochemistry.

~~09/400,992~~



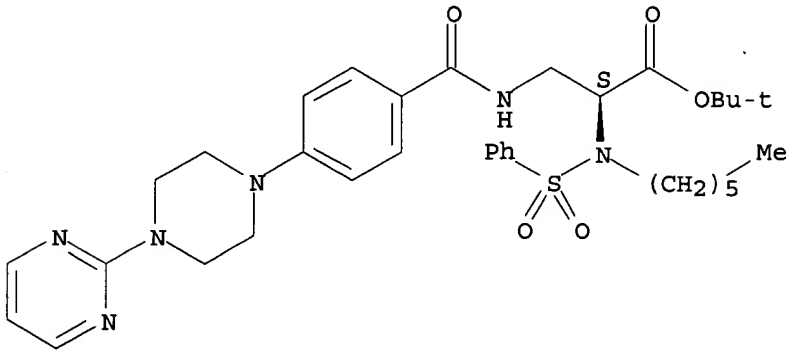
RN 234081-19-7 CAPLUS
CN L-Alanine, N-methyl-N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-21-1 CAPLUS
CN L-Alanine, N-hexyl-N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

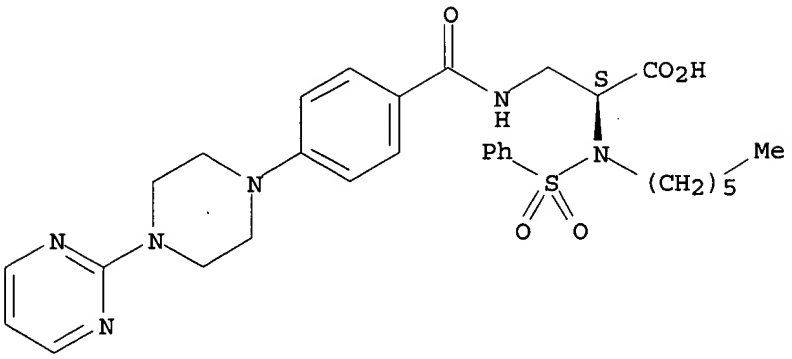
Absolute stereochemistry.



RN 234081-22-2 CAPLUS
CN L-Alanine, N-hexyl-N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

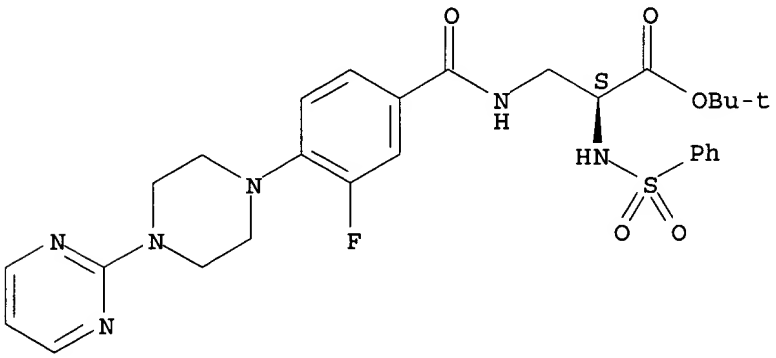
~~09/400,992~~

Absolute stereochemistry.



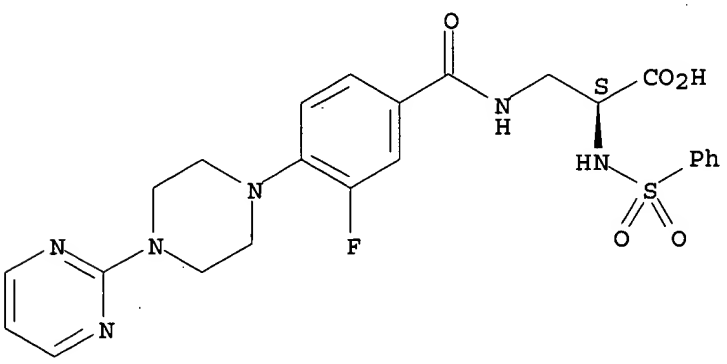
RN 234081-25-5 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



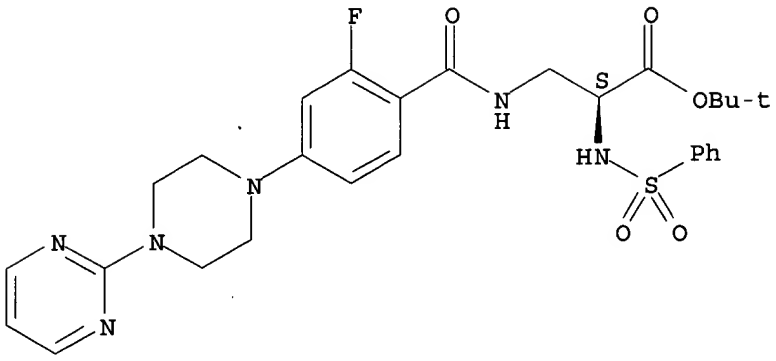
RN 234081-26-6 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



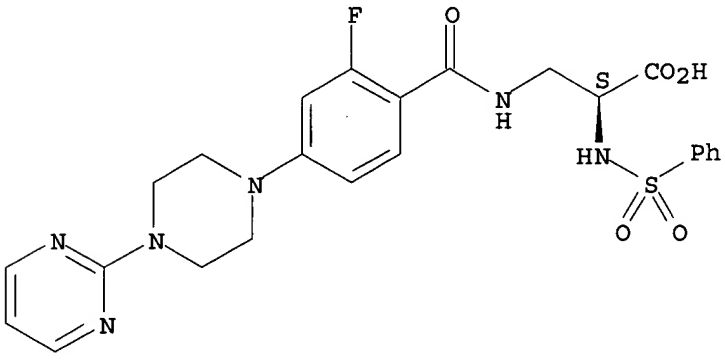
RN 234081-28-8 CAPLUS
CN L-Alanine, 3-[[2-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



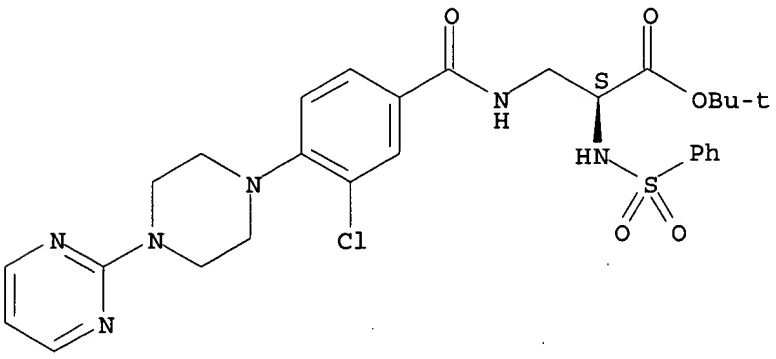
RN 234081-29-9 CAPLUS
CN L-Alanine, 3-[[2-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



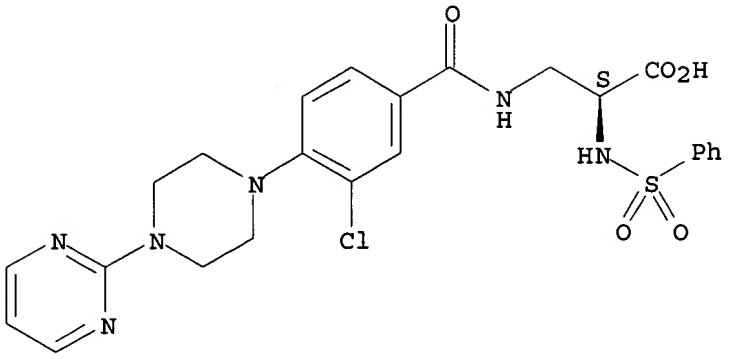
RN 234081-31-3 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



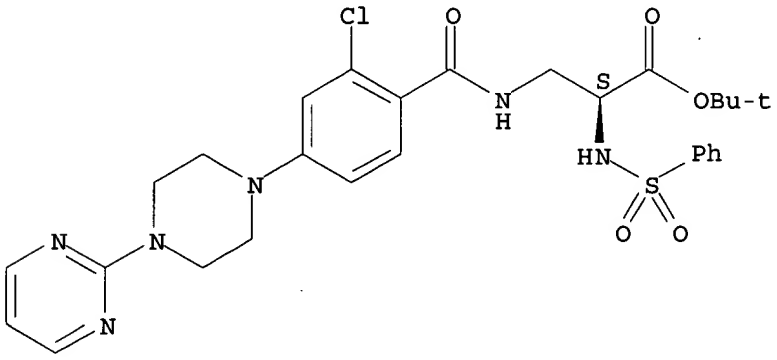
RN 234081-32-4 CAPLUS
CN L-Alanine, 3-[[3-chloro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



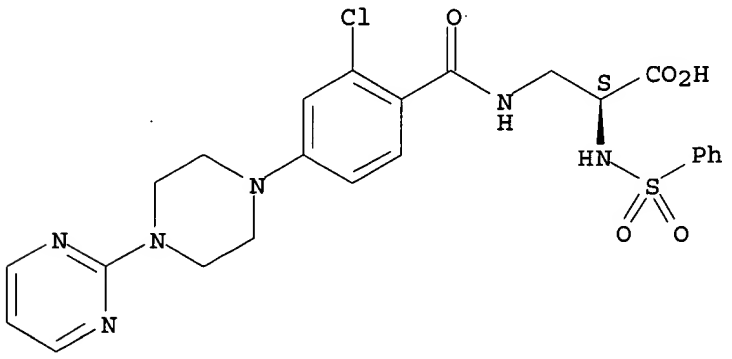
RN 234081-34-6 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



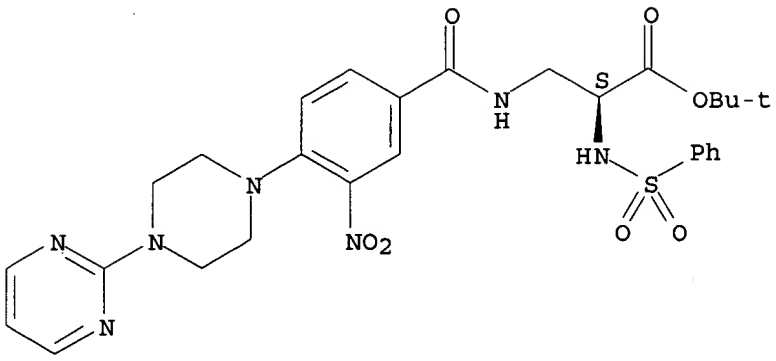
RN 234081-35-7 CAPLUS
CN L-Alanine, 3-[[2-chloro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



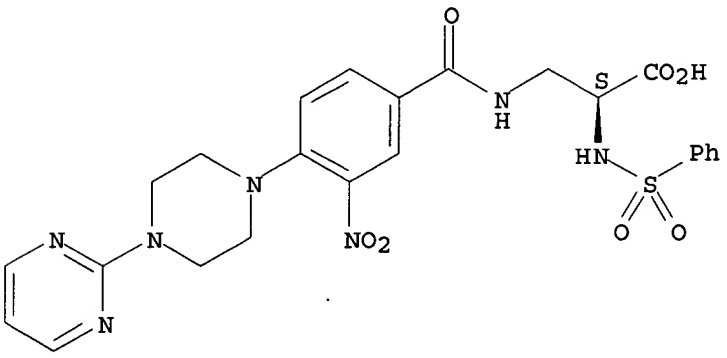
RN 234081-37-9 CAPLUS
CN L-Alanine, 3-[[3-nitro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



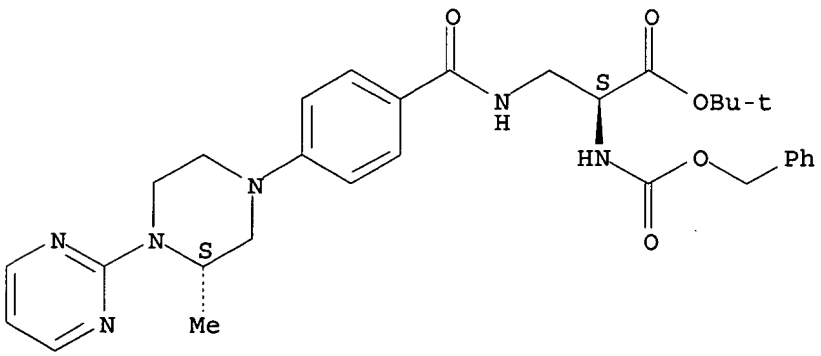
RN 234081-38-0 CAPLUS
CN L-Alanine, 3-[[3-nitro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-40-4 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

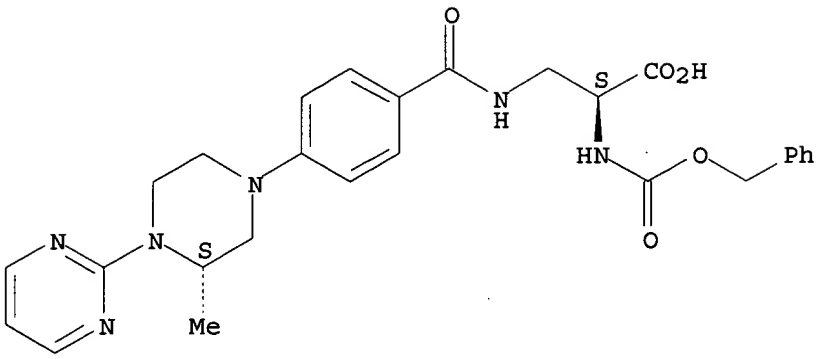
Absolute stereochemistry.



RN 234081-41-5 CAPLUS
CN L-Alanine, 3-[[4-[(3S)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX

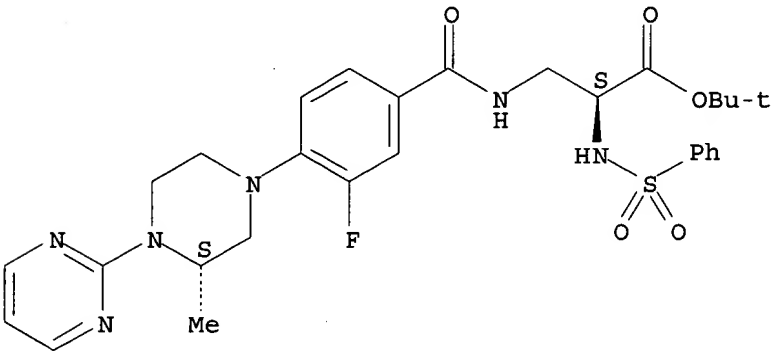
NAME)

Absolute stereochemistry.



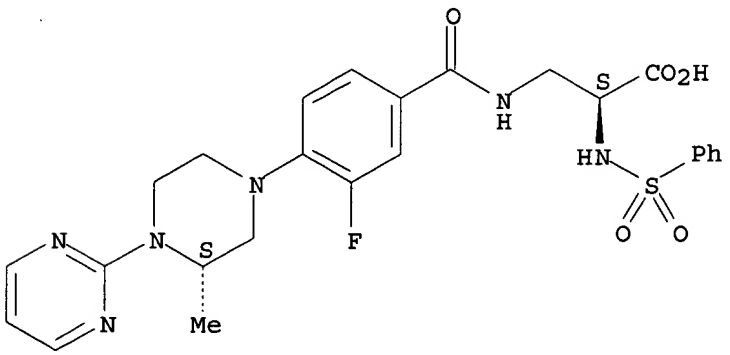
RN 234081-44-8 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3S)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-45-9 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[(3S)-3-methyl-4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-(phenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-47-1 CAPLUS

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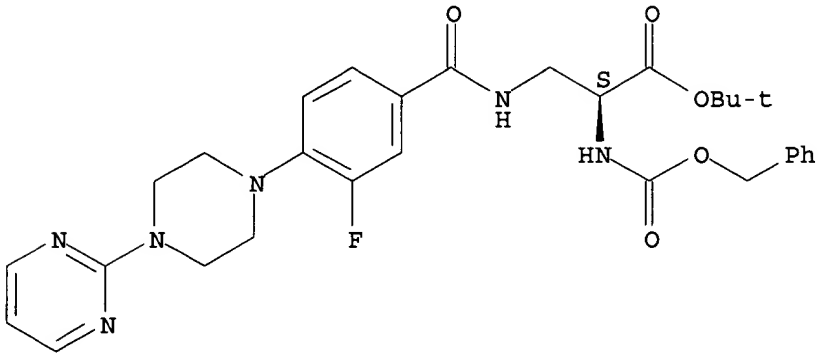
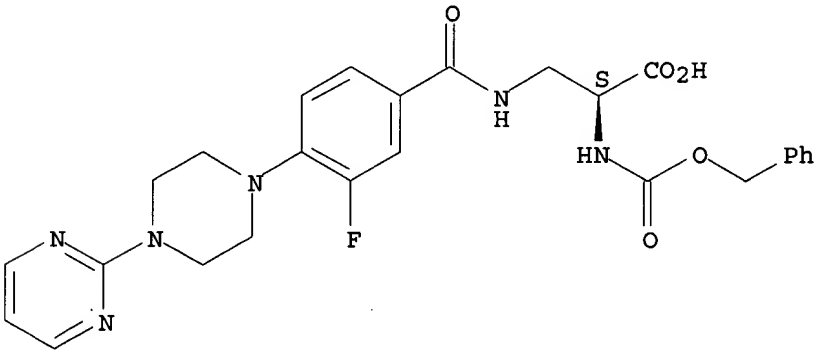
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



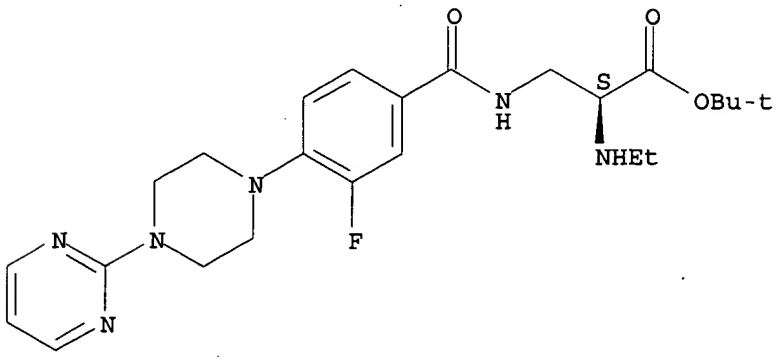
RN 234081-48-2 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 234081-52-8 CAPLUS
CN L-Alanine, N-ethyl-3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

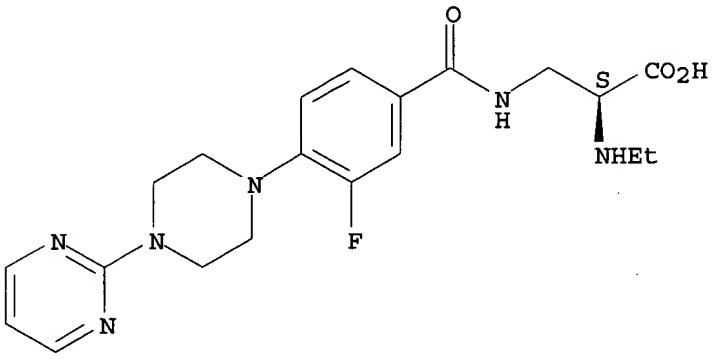
Absolute stereochemistry.



~~09/400,992~~

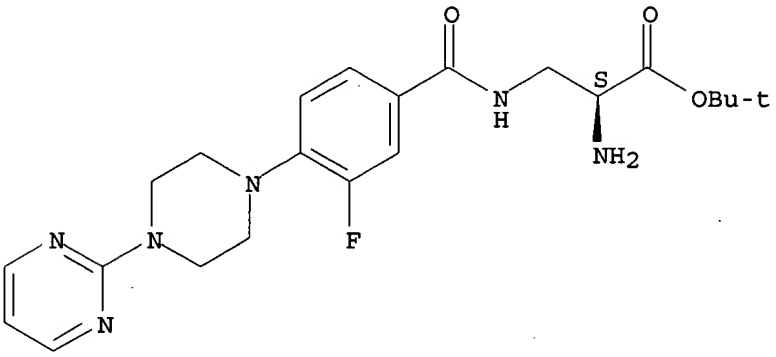
RN 234081-54-0 CAPLUS
CN L-Alanine, N-ethyl-3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



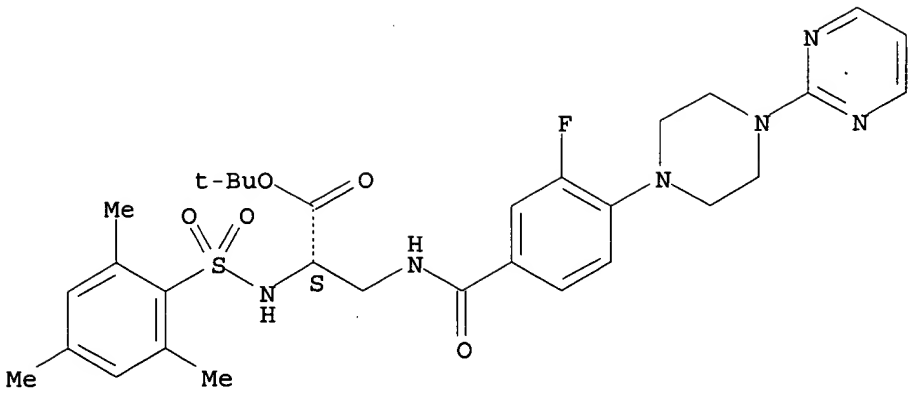
RN 234081-58-4 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



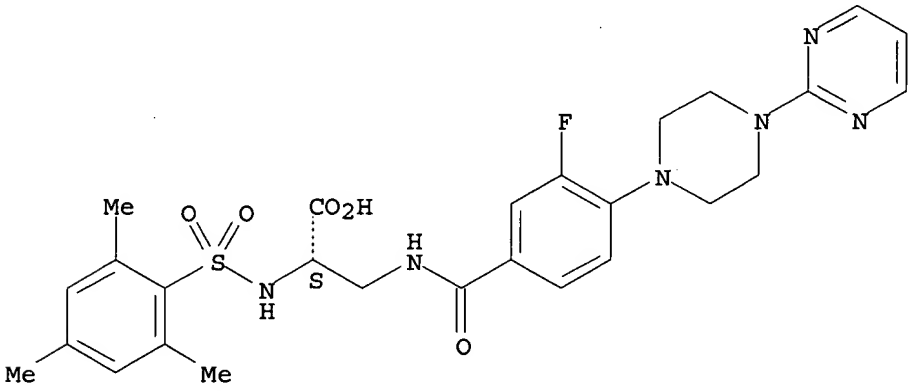
RN 234081-60-8 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



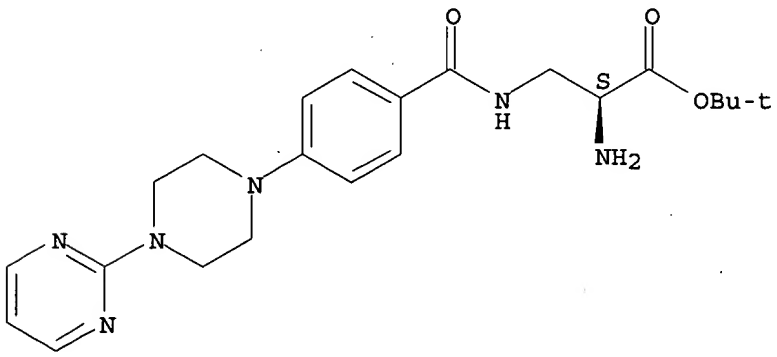
RN 234081-62-0 CAPLUS
CN L-Alanine, 3-[[3-fluoro-4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



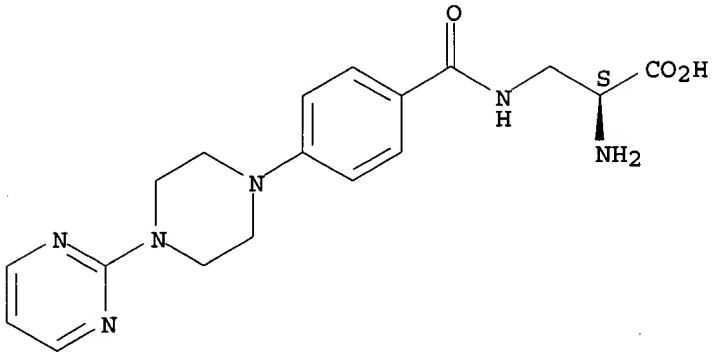
RN 234081-66-4 CAPLUS
CN L-Alanine, 3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

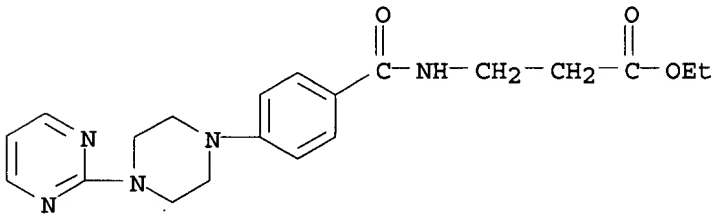


RN 234081-68-6 CAPLUS
CN L-Alanine, 3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]- (9CI) (CA INDEX NAME)

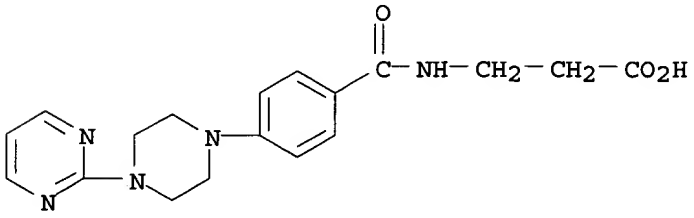
Absolute stereochemistry.



RN 234081-70-0 CAPLUS
CN .beta.-Alanine, N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 234081-71-1 CAPLUS
CN .beta.-Alanine, N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:404930 CAPLUS
DOCUMENT NUMBER: 131:58766
TITLE: Heterocyclic-substituted carboxylic acid **integrin** receptor antagonists
INVENTOR(S): Askew, Ben C.; Coleman, Paul J.; Duggan, Mark E.; Halczenko, Wasyl; Hartman, George D.; Hunt, Cecilia; Hutchinson, John H.; Meissner, Robert S.; Patane, Michael A.; Smith, Garry R.; Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 249 pp.
CODEN: PIXXD2

~~09/400,992~~

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931061	A1	19990624	WO 1998-US26484	19981214
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315220	AA	19990624	CA 1998-2315220	19981214
AU 9918220	A1	19990705	AU 1999-18220	19981214
AU 739811	B2	20011018		
EP 1040098	A1	20001004	EP 1998-963136	19981214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9813769	A	20001010	BR 1998-13769	19981214
EE 200000362	A	20011217	EE 2000-200000362	19981214
JP 2002508355	T2	20020319	JP 2000-538988	19981214
NZ 504893	A	20021025	NZ 1998-504893	19981214
US 6048861	A	20000411	US 1998-212082	19981215
US 6297249	B1	20011002	US 1999-453847	19991202
NO 2000003114	A	20000816	NO 2000-3114	20000616
US 2002010176	A1	20020124	US 2001-916977	20010728

PRIORITY APPLN. INFO.:

US 1997-69899P	P	19971217
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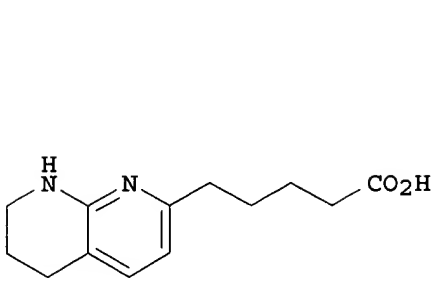
US 1998-83209P	P	19980427
GB 1998-11295	A	19980526
US 1998-92622P	P	19980713
US 1998-108063P	P	19981112
WO 1998-US26484	W	19981214
US 1998-212082	A3	19981215
US 1999-454847	A3	19991207

OTHER SOURCE(S): MARPAT 131:58766
GI

09/400,992



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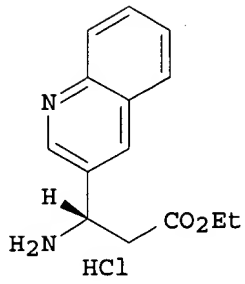

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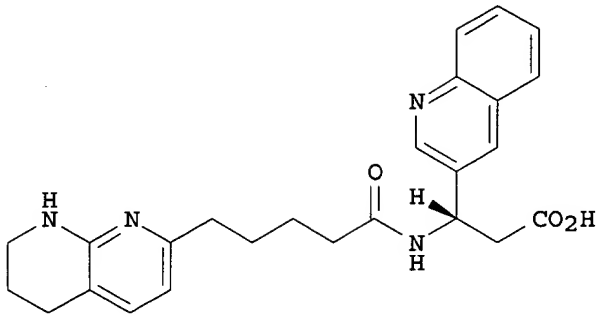

III

AB The substituted carboxylic acids R-X-X1-CR5R6-CR7R8-CO2R9 [R = R1R2NC(:NR1), R1R2NC(:NR1)NR1, 5- or 6-membered nitrogen, oxygen, and/or sulfur heterocyclyl with nitrogen substituted by R1; X = (CH2)m, (CH2)mO(CH2)n, (CH2)mNR4(CH2)n, (CH2)mS(CH2)n, (CH2)mSO(CH2)n, (CH2)mO(CH2)nO(CH2)p, (CH2)mO(CH2)nNR4(CH2)p, etc.; X1 = -CONR4-, -NR4CO-, -NR4CONR4-; and -CH2CH2- or -CH:CH- substituted by R3; R1, R2 = H, halo, alkyl, cycloalkyl, amino, acylamino, alkoxycarbonyl, F3CO, alkylsulfonylamino, etc.; R3 = H, aryl, alkyl, arylalkoxyalkyl, arylalkylaminoalkyl, halo, F3C, H2N, arylaminocarbonyl, etc.; R4 = H, aryl, H2NCO, alkyl, arylalkyl, aryloxycarbonyl, H2SO2, arylsulfonyl, etc.; R5, R6, R7, R8 = H, alkyl, aryl, arylalkoxyalkyl, arylalkylaminoalkyl, halo, HO, H2N, H2NCO, etc.; R9 = H, alkyl, aryl, alkylaminocarbonylmethylene, etc.] and their pharmaceutically acceptable salts were prepd for use as **integrin** receptor antagonists (no data). Thus, amidation of the tetrahydronaphthyridinylpentanoate I with the aminoquinolinepropionate II and subsequent sapon. gave the (quinolinyl)naphthyridinylpentanoylaminopropionate III. More particularly, the compds. of the present invention are antagonists of the **integrin** receptors .alpha..nu..beta.3, .alpha..nu..beta.5, and/or .alpha..nu..beta.6 and are useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, clear degeneration, angiogenesis, atherosclerosis, inflammation, wound healing, viral disease, tumor growth, and metastasis.

IT **227752-23-0P 227752-24-1P 227752-52-5P**
227753-44-8P 227753-45-9P 227753-46-0P
227753-47-1P 227753-48-2P 227753-49-3P
227753-50-6P 227753-51-7P 227753-52-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of heterocyclic-substituted carboxylic acids as **integrin** receptor antagonists)

RN 227752-23-0 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

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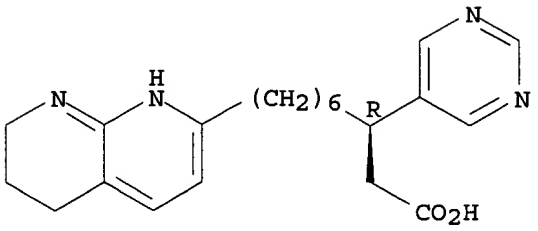
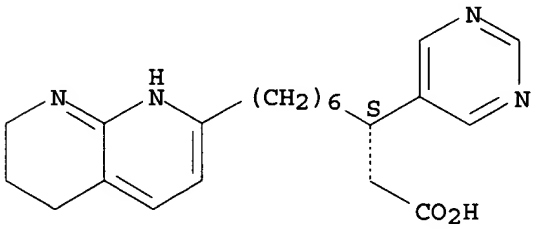
Absolute stereochemistry.



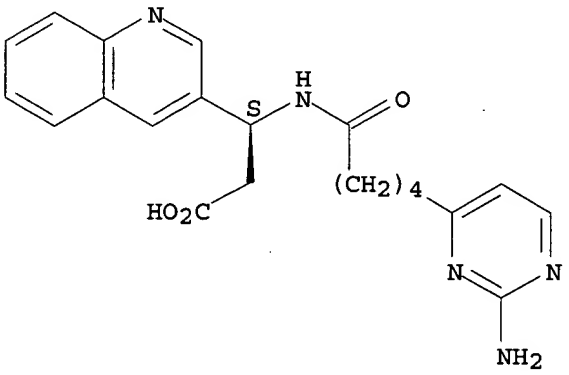
RN 227752-24-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 227752-52-5 CAPLUS
CN 3-Quinolinepropanoic acid, .beta.-[[5-(2-amino-4-pyrimidinyl)-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 227753-44-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 227753-43-7
CMF C21 H28 N4 O2

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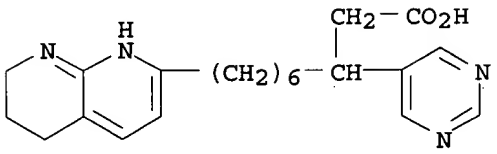
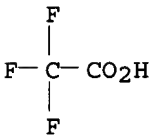


CM 2

CRN 76-05-1
CMF C2 H F3 O2

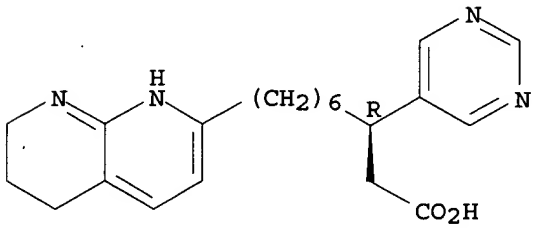


RN 227753-45-9 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

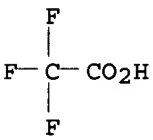
CRN 227752-23-0
CMF C21 H28 N4 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 227753-46-0 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

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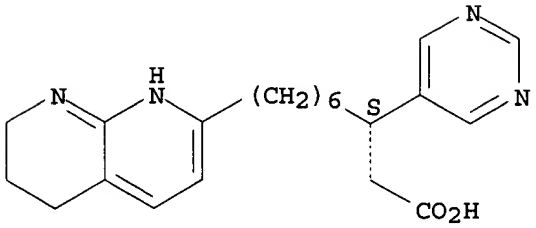
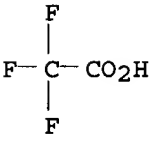
CRN 227752-24-1
CMF C21 H28 N4 O2

Absolute stereochemistry.

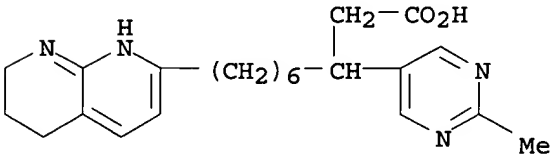


CM 2

CRN 76-05-1
CMF C2 H F3 O2

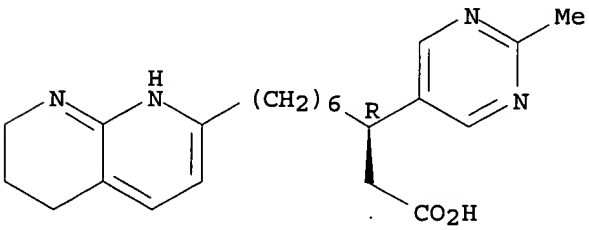


RN 227753-47-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



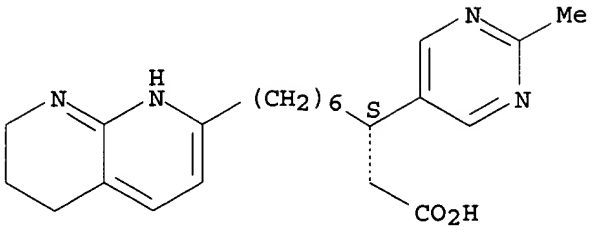
RN 227753-48-2 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

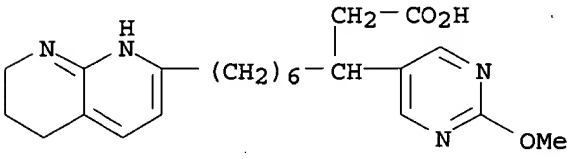


RN 227753-49-3 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

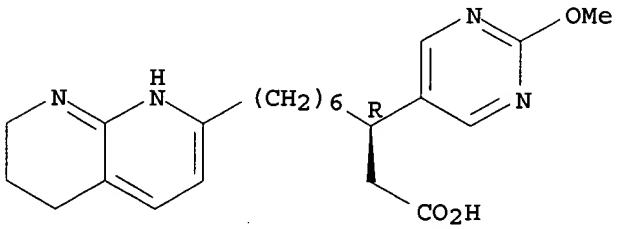


RN 227753-50-6 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



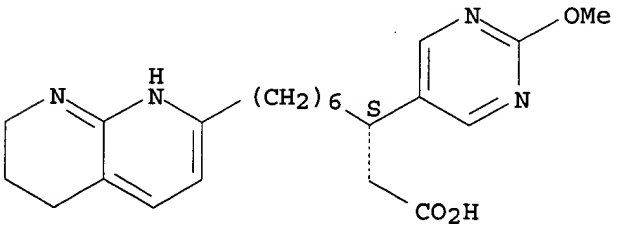
RN 227753-51-7 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 227753-52-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:677821 CAPLUS
DOCUMENT NUMBER: 129:302890
TITLE: Treatment of cancer using a combination of

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integrin antagonists and farnesyl protein transferase inhibitors.

INVENTOR(S): Duggan, Mark E.; Hartman, George D.; Heimbrook, David C.; Oliff, Allen I.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 422 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844797	A1	19981015	WO 1998-US6823	19980406
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869532	A1	19981030	AU 1998-69532	19980406
AU 724216	B2	20000914		
EP 973396	A1	20000126	EP 1998-915318	19980406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001524079	T2	20011127	JP 1998-543013	19980406

PRIORITY APPLN. INFO.: US 1997-41923P P 19970407
GB 1998-976 A 19980116
WO 1998-US6823 W 19980406

OTHER SOURCE(S): MARPAT 129:302890

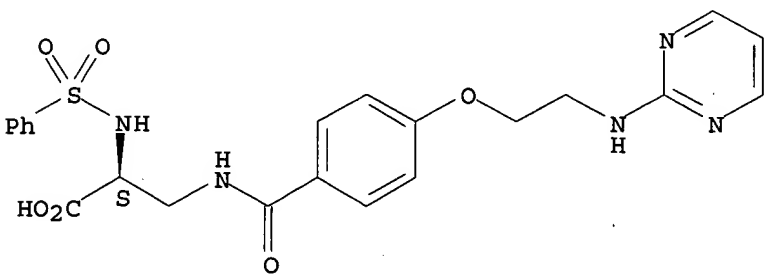
AB A method of achieving a therapeutic effect comprising administration of an **integrin** antagonist and a farnesyl-protein transferase inhibitor where the amt. of either alone is insufficient to achieve the effect, is claimed (no data). Amino acid and peptide derivs., e.g., N-[(2R)-amino-3-mercaptopropyl]valylisoleucylleucine, were prepd.

IT **174665-30-6 174665-57-7 174665-64-6 174665-65-7 206997-23-1 206997-24-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); **BIOL (Biological study)**; USES (Uses)
(treatment of cancer using a combination of **integrin** antagonists and farnesyl protein transferase inhibitors)

RN 174665-30-6 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174665-57-7 CAPLUS

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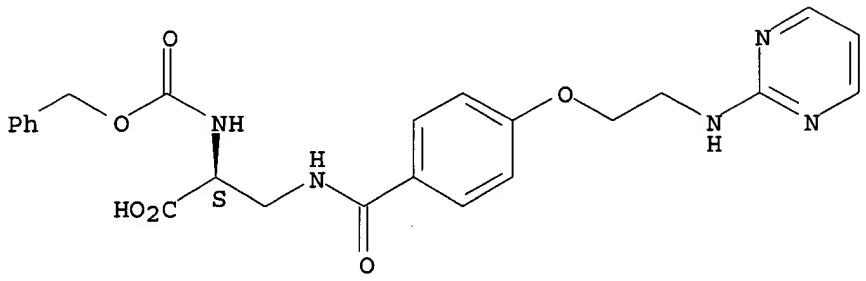
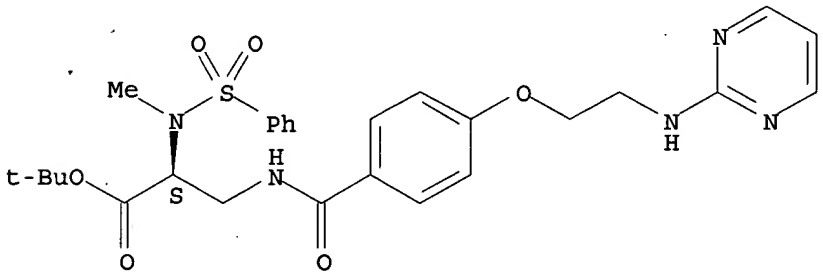
CN L-Alanine, N-[(phenylmethoxy)carbonyl]-3-[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



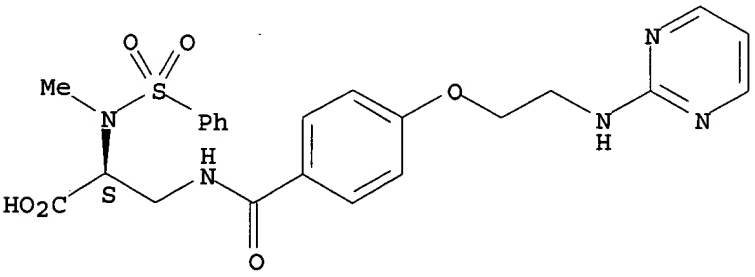
RN 174665-64-6 CAPLUS
CN L-Alanine, N-methyl-N-(phenylsulfonyl)-3-[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174665-65-7 CAPLUS
CN L-Alanine, N-methyl-N-(phenylsulfonyl)-3-[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 206997-23-1 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[6-[(2-pyrimidinylamino)methyl]-2-naphthalenyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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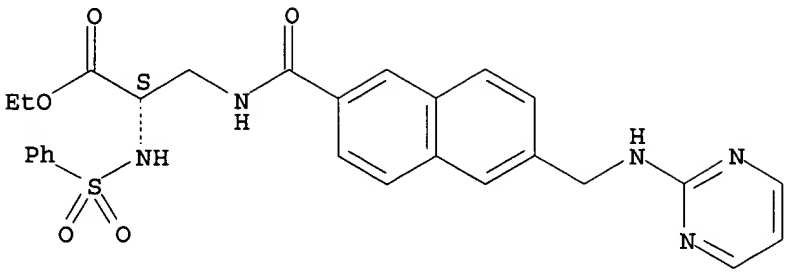
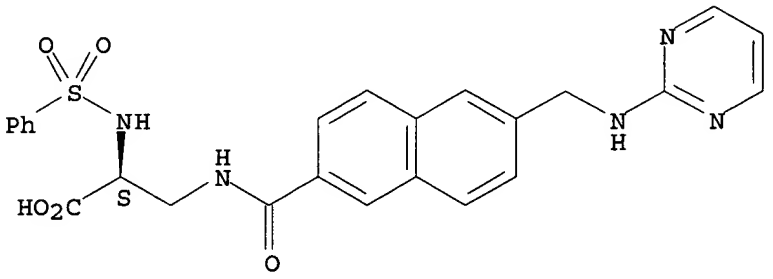


RN 206997-24-2 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[6-[(2-pyrimidinylamino)methyl]-2-naphthalenyl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:293369 CAPLUS
DOCUMENT NUMBER: 128:321934
TITLE: Preparation of amino acid derivatives as **integrin** antagonists
INVENTOR(S): Duggan, Mark E.; Hartman, George D.; Hoffman, William F.; Ihle, Nathan C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Duggan, Mark E.; Hartman, George D.; Hoffman, William F.; Ihle, Nathan C.
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818461	A1	19980507	WO 1997-US19349	19971027
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9850884	A1	19980522	AU 1998-50884	19971027
AU 717283	B2	20000323		
EP 946164	A1	19991006	EP 1997-913775	19971027

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

JP 2001504456	T2	20010403	JP 1998-520639		19971027
US 5919792	A	19990706	US 1997-959662		19971028
PRIORITY APPLN. INFO.:			US 1996-29223P	P	19961030
			GB 1996-26308	A	19961218
			WO 1997-US19349	W	19971027

OTHER SOURCE(S): MARPAT 128:321934

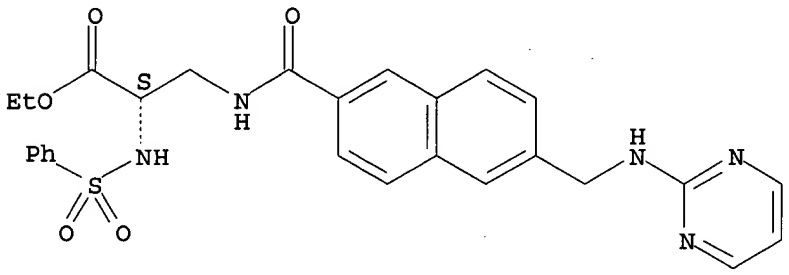
AB Amino acids derivs. X-Y-Z-Ring-A-B [Ring is a mono- or polycyclic ring system; X = NR1R2, NR1CR3:NR2, C(:NR2)NHR4, NR1C(:NR2)NR3R4, aryl-NR1R2, aryl-C(:NR1)NR2R3, aryl-NR1C(:NR2)NR3R4, (R1-R4 = H, halo, alkyl, arylalkyl, aminoalkyl, etc.), a mono- or polycyclic ring system; Y = alkylene, imino-, carbonyl-, oxydialkylene, etc.; Z = (CH2)m, (CH2)mO(CH2)n, (CH2)mC.tplbond.C(CH2)n, etc. (m, n = 0-6); A = (CH2)qO(CH2)p, (CH2)qCS(CH2)p (p, q = 0-6), etc.; B = (un)substituted carboxy- or carbamoylalkyl, including amino acid residues] were prepd. as vitronectin receptor antagonists. Thus, 4-[2-(2-aminopyridin-6-yl)ethyl]benzoyl-2(S)-[[(4-125iodophenyl)sulfonyl]amino]-.beta.-alanine was prepd. and used in a formulation for inhibition of bone resorption.

IT **206997-23-1P 206997-24-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of amino acid derivs. as **integrin** antagonists)

RN 206997-23-1 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[[6-[(2-pyrimidinylamino)methyl]-2-naphthalenyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

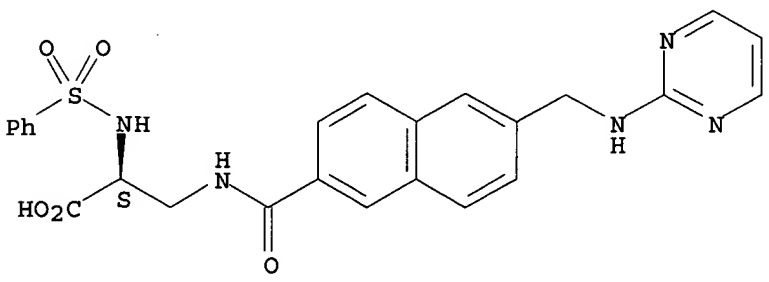
Absolute stereochemistry.



RN 206997-24-2 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[[6-[(2-pyrimidinylamino)methyl]-2-naphthalenyl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:674730 CAPLUS

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DOCUMENT NUMBER: 127:341553
TITLE: The in vitro and in vivo pharmacological profiles of a platelet glycoprotein IIb/IIIa antagonist, NSL-9403
AUTHOR(S): Katada, Jun; Takiguchi, Yoshimi; Muramatsu, Michiko; Fujiyoshi, Toshio; Uno, Isao
CORPORATE SOURCE: Advanced Technology Research Laboratories, Life Science Research Center, Nippon Steel Corporation, Kawasaki, 211, Japan
SOURCE: Thrombosis Research (1997), 88(1), 27-40
CODEN: THBRAA; ISSN: 0049-3848
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

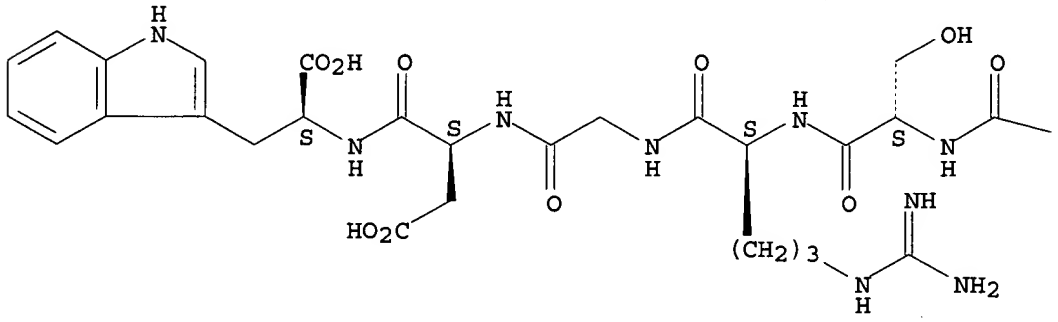
AB The in vitro and in vivo pharmacol. profiles of NSL-9403 [orotyl-seryl-arginyl-glycyl-aspartyl-tryptophane], a platelet glycoprotein IIb/IIIa (GpIIb/IIIa) antagonist, has been studied. NSL-9403 inhibited platelet aggregation of human platelet-rich plasma (PRP) with IC50 values of 4.3 .mu.M (collagen) and 1.8 .mu.M (ADP), which was about 100 times more potent than RGDS. It also inhibited the binding of fibrinogen to activated platelets. Ex vivo collagen and ADP-induced platelet aggregation in a guinea pig was inhibited after a bolus i.v. administration of NSL-9403 at 1.25 mg/kg and above. NSL-9403 had an antithrombotic effect in in vivo thrombosis models. In a platelet agonist-induced pulmonary embolic sudden death model, where a bolus injection of collagen and epinephrine induced sudden death in mice, i.v. administration of NSL-9403 before an injection of collagen and epinephrine inhibited this platelet-agonist induced death in a dose dependent manner. In an arterio-venous shunt, infusion of NSL-9403 at 3 mg/kg/h prevented an increase in circulation pressure due to thrombus formation in the shunt circuit and platelet loss. Infusion of NSL-9403 at 1 to 10 mg/kg/h produced a complete inhibition of platelet-dependent arterial thrombosis in a dog femoral arterial thrombosis model. Thus NSL-9403 is a potent inhibitor or platelet aggregation in vitro and a potent anti-thrombotic agent in vivo with a relatively short duration of action.

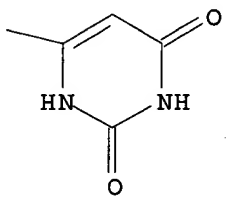
IT **158183-57-4**, NSL-9403
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); **BIOL (Biological study)**; USES (Uses)
(in vitro and in vivo pharmacol. profiles of a platelet glycoprotein IIb/IIIa antagonist NSL-9403)

RN 158183-57-4 CAPLUS
CN L-Tryptophan, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinecarbonyl-L-seryl-L-arginylglycyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L7 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:290093 CAPLUS
DOCUMENT NUMBER: 126:264011
TITLE: Preparation of meta-guanidine, urea, thiourea or azacyclic amino benzoic acid derivatives as **integrin** antagonists
INVENTOR(S): Ruminski, Peter Gerrard; Clare, Michael; Collins, Paul Waddell; Desai, Bipinchandra Nanubhai; Lindmark, Richard John; Rico, Joseph Gerace; Rogers, Thomas Edward; Russell, Mark Andrew; et al.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA; Ruminski, Peter Gerrard; Clare, Michael; Collins, Paul Waddell; Desai, Bipinchandra Nanubhai; Lindmark, Richard, John
SOURCE: PCT Int. Appl., 930 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708145	A1	19970306	WO 1996-US13500	19960827
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2230209	AA	19970306	CA 1996-2230209	19960827
AU 9671039	A1	19970319	AU 1996-71039	19960827
AU 702487	B2	19990225		
EP 850221	A1	19980701	EP 1996-932142	19960827
EP 850221	B1	20010718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1201454	A	19981209	CN 1996-197911	19960827
CN 1085980	B	20020605		
BR 9610422	A	19990713	BR 1996-10422	19960827
JP 11510814	T2	19990921	JP 1996-510397	19960827
IL 123164	A1	20010319	IL 1996-123164	19960827
AT 203234	E	20010815	AT 1996-932142	19960827
ES 2161373	T3	20011201	ES 1996-932142	19960827
NO 9800817	A	19980424	NO 1998-817	19980226

PRIORITY APPLN. INFO.: US 1995-3277P P 19950830
WO 1996-US13500 W 19960827
OTHER SOURCE(S): MARPAT 126:264011

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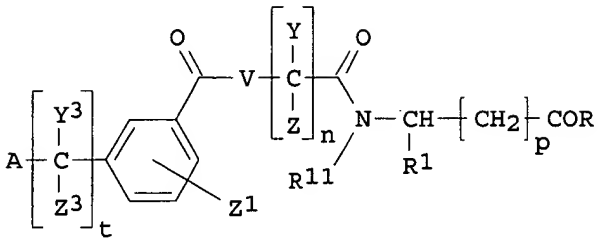
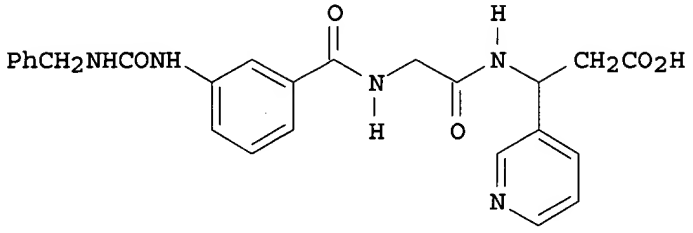
GI



I



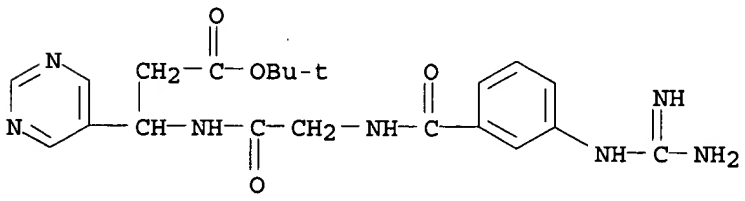
II

AB The title compds. I [A = (un)substituted ureido, guanidino, etc. (generic structures given); Z1 = H, alkyl, OH, alkoxy, halo, (di)(alkyl)amino, aryl, etc.; V = NR6; R6 = H, alkyl, etc.; or YR6 forms a 4- to 12-membered mono-N-contg. ring; Y, Y3, Z, Z3 = H, alkyl, aryl, cycloalkyl; or YZ or Y3Z3 form cycloalkyl; n = 1-3; t = 0-2; p = 0-3; R = XR3; X = O, S, NH, etc.; R3 = H, alkyl, etc.; R1 = H, alkyl, alkenyl, etc.; R11 = H, alkyl, aralkyl, etc.] are prepd. For example, m-nitrohippuric acid was subjected to a sequence of (1) amidation with Et 3-amino-3-(3-pyridyl)propanoate-2HCl; (2) hydrogenation of the nitro group; (3) reaction of the formed amine with benzyl isocyanate; and (4) alk. sapon. of the ester, to give title compd. II, isolated as the CF3CO2H or HCl salt. In an in vitro assay for antagonism of human vitronectin receptor (.alpha.V.beta.3), the title compd. II.HCl bound with an IC50 of 0.86 nM.

IT **188810-02-8P 188810-03-9P 188810-72-2P**
188810-73-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of meta-guanidino, -ureido, -thioureido, or -azacyclic-amino benzoic acid derivs. as **integrin** antagonists)

RN 188810-02-8 CAPLUS

CN .beta.-Alanine, N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(5-pyrimidinyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

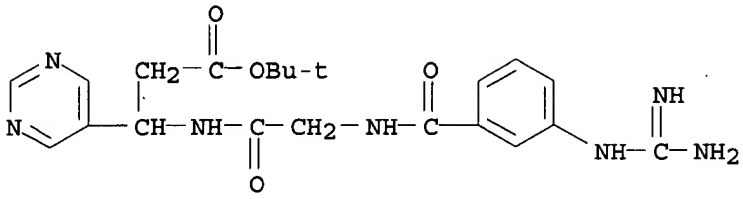


RN 188810-03-9 CAPLUS

CN .beta.-Alanine, N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(5-pyrimidinyl)-, 1,1-dimethylethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

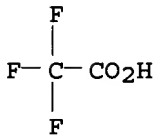
CM 1

CRN 188810-02-8
CMF C21 H27 N7 O4



CM 2

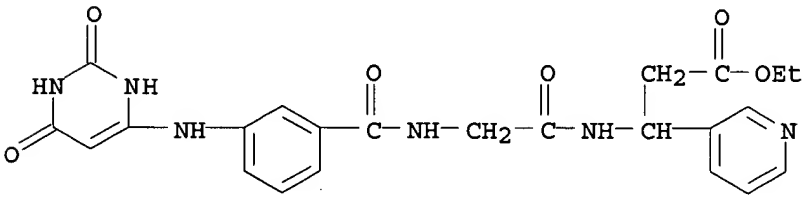
CRN 76-05-1
CMF C2 H F3 O2



RN 188810-72-2 CAPLUS
CN .beta.-Alanine, N-[3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)amino]benzoyl]glycyl-3-(3-pyridinyl)-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

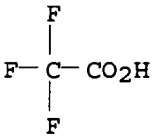
CM 1

CRN 188810-71-1
CMF C23 H24 N6 O6

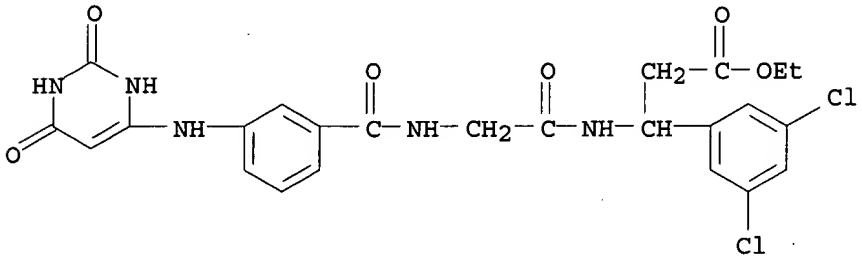


CM 2

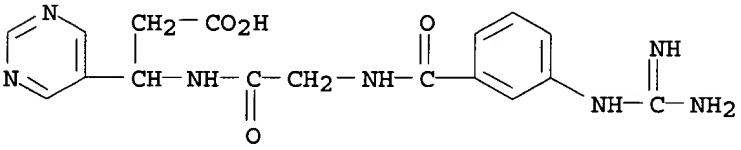
CRN 76-05-1
CMF C2 H F3 O2



RN 188810-73-3 CAPLUS
CN .beta.-Alanine, N-[3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)amino]benzoyl]glycyl-3-(3,5-dichlorophenyl)-, ethyl ester (9CI) (CA INDEX NAME)



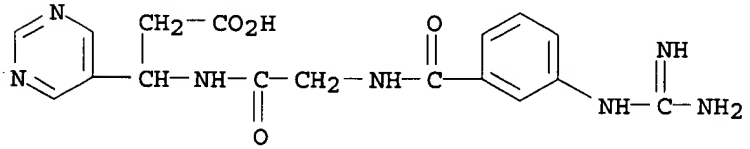
IT **188808-79-9P 188808-80-2P 188809-55-4P**
188809-56-5P 188809-57-6P 188810-71-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); USES (Uses)
(prepn. of meta-guanidino, -ureido, -thioureido, or -azacyclic-amino benzoic acid derivs. as **integrin** antagonists)
RN 188808-79-9 CAPLUS
CN .beta.-Alanine, N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(5-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 188808-80-2 CAPLUS
CN .beta.-Alanine, N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(5-pyrimidinyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

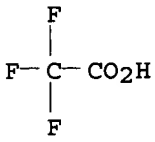
CM 1

CRN 188808-79-9
CMF C17 H19 N7 O4

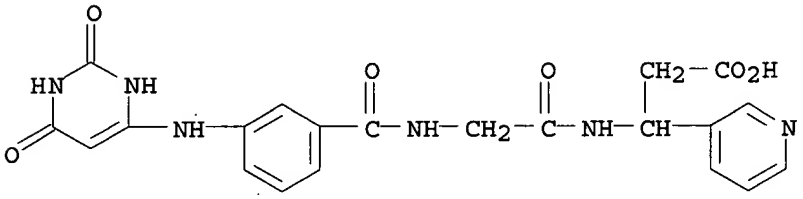


CM 2

CRN 76-05-1
CMF C2 H F3 O2



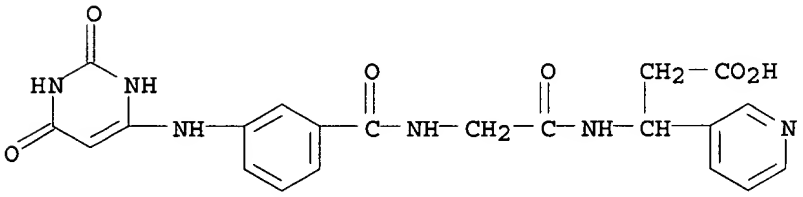
RN 188809-55-4 CAPLUS
CN .beta.-Alanine, N-[3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)amino]benzoyl]glycyl-3-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 188809-56-5 CAPLUS
CN .beta.-Alanine, N-[3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)amino]benzoyl]glycyl-3-(3-pyridinyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

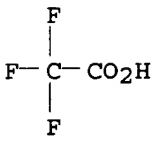
CM 1

CRN 188809-55-4
CMF C21 H20 N6 O6

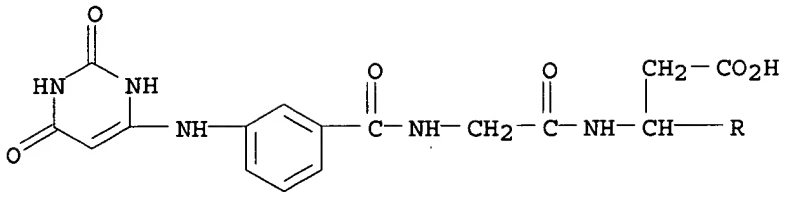


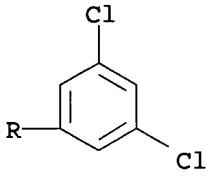
CM 2

CRN 76-05-1
CMF C2 H F3 O2

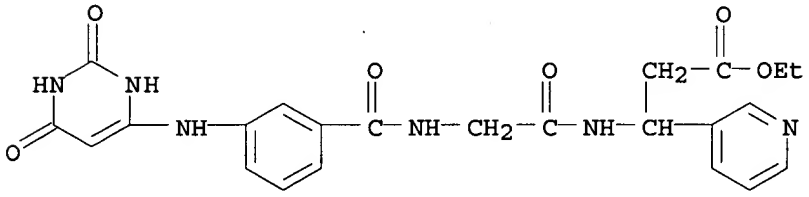


RN 188809-57-6 CAPLUS
CN .beta.-Alanine, N-[3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)amino]benzoyl]glycyl-3-(3,5-dichlorophenyl)- (9CI) (CA INDEX NAME)





RN 188810-71-1 CAPLUS
CN .beta.-Alanine, N-[3-[(1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinyl)amino]benzoyl]glycyl-3-(3-pyridinyl)-, ethyl ester (9CI) (CA INDEX NAME)



L7 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:398904 CAPLUS
DOCUMENT NUMBER: 125:131630
TITLE: Design and synthesis of new antagonist peptides for platelet GPIIb/IIIa receptor as anti-thrombotic agents
AUTHOR(S): Hayashi, Uoshio; Sato, Yoshimi; Katada, Jun; Takiguchi, Yoshimi; Ojima, Iwao; Uno, Isao
CORPORATE SOURCE: Life Sci. Res. Center, Nippon Steel Corporation, Kawasaki, 211, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(12), 1351-1356
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structure-activity relationships of N-terminal modified RGD peptides against platelet aggregation inhibitory activity were studied, and Orotyl-Ser-Arg-Gly-Asp-Trp (NSL-9403) was a new and effective anti-thrombotic agent during extracorporeal circulation.
IT **158183-57-4P**, NSL-9403
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); **BIOL (Biological study)**; PREP (Preparation); PROC (Process); USES (Uses)
(design and synthesis of new antagonist peptides for platelet GPIIb/IIIa receptor as anti-thrombotic agents in relation to structure)
RN 158183-57-4 CAPLUS
CN L-Tryptophan, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinecarbonyl-L-seryl-L-

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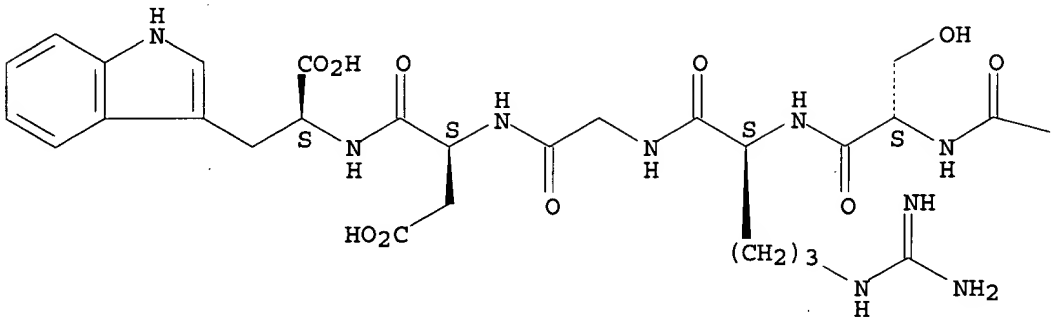
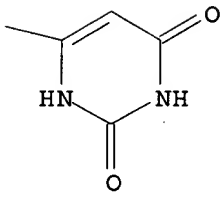
arginylglycyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L7 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:328908 CAPLUS
DOCUMENT NUMBER: 122:240416
TITLE: Design of orally active, non-peptide fibrinogen receptor antagonists. An evolutionary process from the RGD sequence to novel antiplatelet aggregation agents
AUTHOR(S): Bovy, P. R.; Tjoeng, F. S.; Rico, J. G.; Rogers, T. E.; Lindmark, R. J.; Zablocki, J. A.; Garland, R. B.; McMackins, D. E.; Dayringer, H.; et al.
CORPORATE SOURCE: Thrombosis Research, Searle, Skokie, IL, 60077, USA
SOURCE: Bioorganic & Medicinal Chemistry (1994), 2(9), 881-95
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

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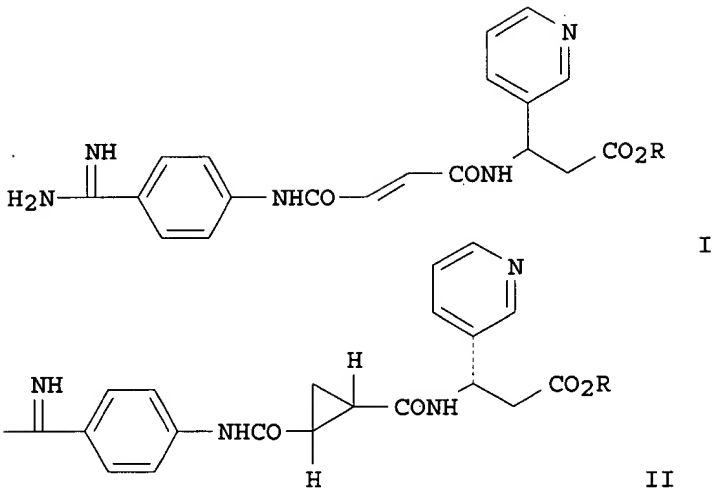

I

II

AB The evolutionary process from the Arg-Gly-Asp-Phe (RGDF) tetrapeptide to potent orally active antiplatelet agents is presented. The RGD sequence is an important component in the recognition of fibrinogen by its platelet receptor GP IIb-IIIa (**integrin** .alpha.IIb.beta.3). This work concs. on the replacement of the Arg-Gly dipeptidyl fragment by an acylated aminobenzamidine. The C-terminal fragment has been replaced by a variety of .beta.-amino acids, expanding on a previously reported paradigm. The lead compds. showed good potency in an in vitro platelet aggregation assay (dog PRP/ADP). The affinity for the fibrinogen receptor was confirmed in several cases by the ability to inhibit 235I fibrinogen binding to activated human platelets. The Et ester prodrug form was tested by oral administration to dogs and monitoring of the anti-platelet effect on ex vivo collagen induced platelet aggregation. From the structural studies reported, the (amidinophenyl)succinamic acid deriv. 4-[HN:C(NH2)]C6H4NHCOCH2CH2CO2H was the best surrogate for the Arg-Gly dipeptide. Several conformationally restricted analogs are also reported which are compatible with the hypothesis of RGD binding to the .alpha.IIb.beta.3 in a turn-extended-turn conformation. The structure-activity relationships described also underline the importance of the .beta.-amino acid substitution for potency. In particular, the abs. configuration at the .beta.-carbon was crucial for high affinity. The best acid/ester pairs (I and II; R = H, Et) reported in this study had high potency (R = H; PRP/ADP IC50 .simeq. 50 nM) and showed good oral activity in dogs at 5 mg/kg per os (R = Et).

IT **162146-76-1P 162146-77-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation)
(design and synthesis of orally active nonpeptide fibrinogen receptor antagonists)

RN 162146-76-1 CAPLUS

RN 162146-77-2 CAPLUS

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(FILE 'HOME' ENTERED AT 13:25:25 ON 21 MAR 2003)

FILE 'REGISTRY' ENTERED AT 13:25:33 ON 21 MAR 2003
L1 STRUCTURE UPLOADED
L2 12 S L1
L3 5877 S L1 FUL

~~09/~~ ~~400,992~~

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     FILE 'CAPLUS' ENTERED AT 13:26:13 ON 21 MAR 2003
L4          1325 S L3
L5           552 S L3/BIOL
L6           320 S L3/THU
L7            40 S L5 AND INTEGRIN?

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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                                                       ENTRY    SESSION
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